

24 Hour Summary
Circulatory System Devices Panel
of the
Medical Devices Advisory Committee
The OPTIMZER SMART device (first of its kind)
Tuesday, December 4, 2018

Introduction:

The Circulatory System Devices Panel of the Medical Devices Advisory Committee to the Food and Drug Administration met on Dec 4, 2018 to discuss, make recommendations and vote on information related to the Pre-Market Application for The OPTIMZER SMART device, which is manufactured by Impulse Dynamics (USA), Inc. and is a first of its kind. The device is considered to be a breakthrough device and is indicated to provide cardiac contractility modulation (CCM) for class III heart failure patients who are not responding to optimal medical therapy.

Device Description:

The OPTIMIZER SMART Implantable Pulse Generator (IPG) was designed to deliver Cardiac Contractility Modulation (CCM), which are non-excitatory electrical signals during the myocardial absolute refractory period in synchrony with locally sensed electrical activity. CCM signals are intended to treat patients with moderate to severe symptomatic heart failure despite guideline directed maximal medical therapy. CCM is intended for patients with a narrow QRS who are ineligible for cardiac resynchronization therapy (CRT). In addition to the Implantable Pulse Generator, 3 implantable leads are required to deliver CCM therapy from the IPG to the heart: (1) Sense Lead in the right Atrium and (2) Therapy Delivery Leads (right Ventricle).

The sponsor has proposed the following Indications for Use:

The OPTIMIZER System, which delivers CCM therapy, is indicated for the treatment of NYHA Class III or ambulatory NYHA Class IV heart failure patients who remain symptomatic despite guideline directed medical therapy, are in normal sinus rhythm with LVEF ranging from 25% to 45% and are not indicated for CRT to improve exercise tolerance, quality of life, and functional status.

Panel Deliberations/FDA Questions:

Question 1: Effectiveness

The panel discussed the clinical significance of the effectiveness results, including peak VO₂, Minnesota Living with Heart Failure Questionnaire (MLWHFQ), New York Heart Association (NYHA) class and 6 Minute Hall Walk (6MHW). The panel concluded that the results indicate marginal effectiveness and that there may be a placebo effect. Additional

exploration of who would benefit may be helpful in informing shared decision making between patients and clinicians.

Question 2: Safety

The panel discussed the clinical significance of the safety results, including (a) procedural and device related adverse events, and (b) longer-term heart failure hospitalization and mortality data. The panel concluded that there was a higher than expected lead dislodgement rate but overall the device and procedural risks would be similar to those of a pacemaker device. They agreed there was no inherent safety signal and no differences observed in all-cause mortality between the treatment and control groups. Additionally, the panel noted long-term data is needed to assess complications, specifically to determine if current adverse event rates will decrease over time and review potential interactions with other implantable devices in the intended patient population.

Question 3: Indication for Use

The panel discussed the proposed indications for use. The panel concluded that the clinical results suggest that the claim of improved exercise tolerance should be removed since Peak VO₂ did not improve. They also discussed that the indicated patient population should be limited to patients who have a Peak VO₂ between 9-20 mL/kg/min and NYHA Class III (excluding ambulatory NYHA class IV) patients.

Question 4: Benefits & Risk

The panel discussed if the totality of evidence regarding effectiveness and safety profile of the device indicate that the benefits outweigh the risks of this device. The panel concluded that there is marginal benefit. Therefore, significant consideration should be given to who receives the device. The panel discussed that detailed shared decision making with the patient would be necessary to discuss the benefits and risks of the device. The panel was concerned that younger patients may be exposed to additional risk due to the number of leads and potential needs for revisions and other device procedures over time.

Question 5: Post Approval Study

The panel discussed the proposed post-approval study (PAS). The panel concluded that a longer and larger study would be appropriate to capture both long-term safety and effectiveness data. For example, a study with at least 500 patients with 3-5 years of follow-up may be considered to further inform the labeling in the future. The panel recommended that effectiveness data such as, cardiac outcomes, quality of life, mortality, and functionality be included in endpoint analyses.

Voting Results:

Voting Question 1: Is there reasonable assurance that the OPTIMIZER System is SAFE for use in patients who meet the criteria specified in the proposed indication?

The Advisory Panel Voted: YES: 12
ABSTAIN: 0
NO: 1

Voting Question 2: Is there reasonable assurance that the OPTIMIZER System is EFFECTIVE for use in patients who meet the criteria specified in the proposed indication?

The Advisory Panel Voted: YES: 11
ABSTAIN: 0
NO: 2

Voting Question 3: Do the BENEFITS of the OPTIMIZER System outweigh the RISKS for use in patients who meet the criteria specified in the proposed indication?

The Advisory Panel Voted: YES: 12
ABSTAIN: 1
NO: 0

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