Cardiac contractility modulation

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Policy contains: Cardiac contractility modulation; chronic heart failure.

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Coverage policy

The Implantable Optimizer® Smart System for delivering Cardiac Contractility Modulation™ for moderate to severe chronic heart failure is investigational/not clinically proven and, therefore, not medically necessary.

Limitations

No limitations were identified during the writing of this policy.

Alternative covered services

- Cardiac resynchronization therapy.
- Drug treatment.
- Heart transplant or other surgical intervention.

Background

Heart failure occurs from an inability of the heart to pump sufficient blood and oxygen to support various body organs. About 6.2 million U.S. adults have heart failure, which was mentioned on 379,800 (13.4%) of all 2018 death certificates (Centers for Disease Control and Prevention, 2020).

The New York Heart Association classifies heart failure into four classes, based on degree of ability to function, with Class IV being the most severe. These definitions include:
• **Class I** — No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea (shortness of breath).

• **Class II** — Slight limitation of physical activity. Comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea (shortness of breath).

• **Class III** — Marked limitation of physical activity. Comfortable at rest. Less than ordinary activity causes fatigue, palpitation, or dyspnea.

• **Class IV** — Unable to carry on any physical activity without discomfort. Symptoms of heart failure at rest. If any physical activity is undertaken, discomfort increases (American Heart Association, 2017).

Recent improvements in therapy for heart failure with reduced ejection fractions have reduced morbidity and mortality. However, only one-third of patients meet criteria for the implantable defibrillator (left ventricle ejection fraction ≤ 35%) and for cardiac resynchronization therapy (QRS ≥ 130 ms and evidence of left bundle branch block), and symptoms fail to improve in many patients who do meet criteria (Cappanolli, 2020). The five-year survival rate for heart failure patients with reduced ejection fraction has remained steady in the past several decades at about 50% (Giallauria, 2020).

Impulse Dynamics of Orangeburg, New York, has developed a proprietary technology known as the Implantable Optimizer® Smart System for delivering Cardiac Contractility Modulation™ for treatment of Class III and IV heart failure. The technique works through an electrical pulse delivered during the absolute refractory period, just after the heart contracts. In contrast to a pacemaker or defibrillator, Cardiac Contractility Modulation™ modulates the strength of heart muscle contraction, instead of rhythm (Impulse Dynamics, 2019).

The device is implanted in the right or left pectoral region and is connected to two standard pacemaker leads threaded through veins into the right ventricle, which sense ventricular activity and deliver cardiac contractility modulation signals. An optional additional lead may be used to sense atrial activity (usually placed in the right atrial appendage). Pulses are delivered at regular intervals throughout the day that increase cardiac output or myocardial contractility (Impulse Dynamics, 2018).

On March 21, 2019, the U.S. Food and Drug Administration granted premarket application approval to Impulse Dynamics of the Optimizer Smart System. The government approved the device for New York Heart Association Class III or IV heart failure patients who remain symptomatic after medical therapy, who are in normal sinus rhythm, who are not candidates for cardiac resynchronization therapy, and have a left ventricular ejection fraction from 25% to 45%.

Potential improvement measures include six-minute hall walk distance, quality of life, and functional status. Patients for whom the device is contra-indicated include those 1) with permanent or long-standing persistent atrial fibrillation or flutter; 2) with a mechanical tricuspid valve; and/or 3) for whom vascular access for implantation of the leads cannot be obtained (U.S. Food and Drug Administration, 2019).

**Findings**

The 2017 guideline on heart failure management from the American College of Cardiology, American Heart Association, and Heart Failure Society of America does not include cardiac contractility modulation therapy (Yancy, 2017). The American Association of Family Physicians guideline on heart failure also makes no mention of the device (American Association of Family Physicians, 2020).
A guideline from the United Kingdom found insufficient evidence supporting use of cardiac contractility modulation for heart failure, even suggesting that the technique may be better for patients with less severe heart failure, even though tests to date have only included Class III and IV patients (National Institute for Health and Care Excellence, 2019).

A European Cardiac Society consensus opinion states cardiac contractility modulation may be considered in patients with a left ventricular ejection fraction of 25% to 45%, and a narrow QRS complex < 130 milliseconds to improve exercise capacity, quality of life, and alleviate heart failure function (Seferovic, 2019).

A 2014 report from the European Heart Rhythm Association did not endorse cardiac contractility modulation, but pointed out limits, such as the inability of the (then) version of the device to be used in patients with atrial fibrillation or frequent ectopy. The report also suggested improvements, such as not relying on P-wave detection, enabling use in patients with atrial fibrillation, and developing a device combining the technique with implantable cardioverter-defibrillator functions (Kuck, 2014).

An early trial randomized 428 class III or IV heart failure patients with ejection fraction ≤ 35% to optimal medical therapy, with versus without contractility modulation therapy. Ventilatory anaerobic threshold did not improve after six months of treatment. However, contractility modulation therapy significantly improved peak oxygen consumption ($P = .024$) and Minnesota Living with Heart Failure Questionnaire ($P < .0001$) after six months. There were no adverse effect on hospitalization or mortality rates (Kadish, 2011).

A randomized controlled trial (n = 160) that led to U.S. Food and Drug Administration approval compared heart failure patients given optimal medical treatment with versus without cardiac contractility modulation. After 24 weeks, the group with modulation showed superior results in Minnesota Living with Heart Failure questionnaire ($P < .001$), New York Hospital Association functional class ($P < .001$), and six-minute hall walk distance ($P = .02$). The composite rate of cardiovascular death and heart failure hospitalizations declined from 10.8% to 2.9% ($P = .048$) (Abraham, 2018).

A systematic review/meta-analysis of four randomized controlled trials (n = 801) divided patients into those receiving standard of care with and without the Optimizer device. After a mean follow up of six months, patients with cardiac contractility modulation had superior Minnesota Living with Heart Failure Questionnaire results ($P = .0008$). The study found no differences between groups in heart failure hospitalizations ($P = .12$), all-cause hospitalizations ($P = .33$), six-minute walk distance ($P = .10$), arrhythmias ($P = .14$), pacemaker and implantable cardioverter defibrillator malfunctions ($P = .06$), or all-cause mortality ($P = .92$). Authors state larger trials with longer follow up may be needed to determine benefits of this therapy (Mando, 2019).

A meta-analysis of five controlled trials (n = 861) of cardiac contractility modulation for heart failure revealed superior outcomes after six months for cases versus controls for peak oxygen consumption ($P < .00001$), six-minute walk test distance ($P = .005$), and Minnesota Living with Heart Failure Questionnaire scores ($P < .00001$). Authors state low average patient age in the four largest trials (52, 58, 59, and 63) is a limitation. One author acknowledged receiving honoraria and lecture fees from Impulse Dynamics (Giallauria, 2020).

A meta-analysis of four trials (n = 723) found that cardiac contractility modulation did not significantly improve all-cause mortality or all-cause hospitalizations. The study found no differences in the rate of adverse effects among patients given this treatment, compared with sham or usual care. Significant improvements were observed in peak oxygen consumption ($P = .006$) and the six-minute walk test distance ($P = .049$) (Liu, 2017).
A meta-analysis of three trials (n = 641) documented that compared to controls, cardiac contractility modulation did not significantly improve all-cause mortality ($P = .69$), and did not improve the all-cause hospitalization rate. Authors also did not observe any increase in adverse effects with modulation (Kwong, 2012).

A review of 475 hospitalized heart failure patients in the United Kingdom documents that only 24 (5.1%) meet criteria for cardiac contractility modulation (ejection fraction 25% - 45%, QRS duration < 130 ms, New York Heart Association class III and IV, and treated for heart failure > 90 days on stable medications). Exclusion criteria included significant valvular disease, permanent or persistent atrial fibrillation, biventricular pacing system implanted or QRS duration > 130 ms, and patients not suitable for device therapy due to palliative treatment intent. Heart failure patients with atrial fibrillation represent an additional 3.8% (Dulai, 2021).

**References**

On February 9, 2021, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were “Cardiac Contractility Modulation” and “chronic heart failure.” We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.


**Policy updates**