Prior Authorization Review Panel  
MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review. Policies submitted without this form will not be considered for review.

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<th>Plan: Aetna Better Health</th>
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**Type of Submission – Check all that apply:**
- ☒ New Policy*
- ☐ Revised Policy
- ☐ Annual Review – No Revisions

*All revisions to the policy must be highlighted using track changes throughout the document. Please provide any clarifying information for the policy below:

**CPB 0930 Cardiac Contractility Modulation (CCM) Therapy**

Policy is new to Aetna Better Health of Pennsylvania. This new CPB states that cardiac contractility modulation (CCM) therapy, administered by Impulse Dynamics’ Optimizer system, is considered experimental and investigational because the effectiveness of this approach has not been established.

<table>
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<tr>
<th>Name of Authorized Individual (Please type or print):</th>
<th>Signature of Authorized Individual:</th>
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<tr>
<td>Dr. Bernard Lewin, M.D.</td>
<td>Bernard Lewin, M.D.</td>
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Cardiac Contractility Modulation (CCM) Therapy

Number: 0000

Policy

Aetna considers cardiac contractility modulation (CCM) therapy, administered by Impulse Dynamics’ Optimizer system, experimental and investigational because the effectiveness of this approach has not been established.

See also:

CPB 0585 - Cardioverter-Defibrillators
(http://www.aetna.com/cpb/medical/data/500_599/0585.html)

CPB 0610 - Biventricular Pacing (Cardiac Resynchronization Therapy)/Combination Resynchronization-Defibrillation Devices for Congestive Heart Failure
(http://www.aetna.com/cpb/medical/data/600_699/0610.html)
Background

Impulse Dynamics offers cardiac contractility modulation (CCM) therapy to treat adults with moderate-to-severe “chronic” heart failure that is symptomatic despite optimal medical therapy. CCM delivers non-excitatory electrical signals to the right side of the intraventricular septum during the absolute refractory period of the ventricular contraction, and does not trigger a new action potential. CCM signals are delivered by Impulse Dynamics' Optimizer system (i.e. Optimizer IVs), which is an implantable pulse generator. This device is implanted in a minimally-invasive procedure under local anesthesia, typically in the right pectoral region. CCM has been evaluated in patients with heart failure with reduced ejection fraction (HFrEF) in NYHA Classes II–IV with normal QRS duration (<120 ms). In contrast to a pacemaker or a defibrillator, the system is designed to modulate the strength of contraction of the heart muscle rather than the rhythm. CCM therapy is delivered at regular intervals throughout the day. The "common patient profile" for this therapy is NYHA II-III, normal QRS, EF greater than 20%, peak VO$_2$ $\geq$ 10 mL/kg/min, and ventricular ectopies or bigeminies less than 10000 per day (Impulse Dynamics, 2018).

Some individuals may also require and ICD device, or already have one implanted. The Optimizer IVs is designed to work in parallel with any ICD device and generally does not cause any interruption of ICD function. The Optimizer IVs is contraindicated for patients with permanent or long-standing persistent atrial fibrillation or flutter, mechanical tricuspid valve, no venous
access, and device programmed to 100% VVI pacing (Impulse Dynamics, 2018).

Kadish et al. (2011) conducted a randomized controlled prospective study (FIX-HF-5) to evaluate the safety and efficacy of cardiac contractility modulation (CCM) in advanced heart failure (HF). A total of 428 adults with NYHA class III or IV, narrow QRS (defined as less than 130 msec duration) and EF ≤35% were randomly assigned to receive optimal medical therapy (OMT) plus CCM (n=215), or OMT alone (n=213). The primary efficacy endpoint, required by the U.S. FDA, was the change from baseline in the ventilatory anaerobic threshold (VAT) measured on CPX. Secondary efficacy endpoints were peak Vo2 (pVo2), and quality of life assessed by the Minnesota Living with Heart Failure Questionnaire (MLWFQ) at 6 months. The primary safety end point was a test of non-inferiority between groups at 12 months for the composite of all-cause mortality and hospitalizations through 50 weeks. While VAT did not improve at 6 months, CCM significantly improved pVo2 (P = .024) and MLWHFQ (P < .0001), respectively, over OMT. Forty-eight percent of OMT and 52% of CCM patients experienced a safety end point, which satisfied the non-inferiority criterion (P = .03). Post hoc, hypothesis-generating analysis identified a subgroup (characterized by baseline ≥ 25 and NYHA class III symptoms) in which all parameters were improved by CCM. The authors concluded that further study is required to clarify the role of CCM therapy in refractory heart failure.

Abraham et al. (2015) designed a confirmatory study (the FIX-HF-5C) to prospectively confirm
the efficacy of CCM originally identified in the FIX-HF-5 study of patients with EF 25%–45%. This Impulse Dynamics FIX-HF-5C study is an ongoing, prospective, multicenter, randomized, parallel-controlled trial that is being conducted to evaluate the safety and efficacy of CCM signals delivered by the implantable Optimizer System (specifically the Optimizer IVs) in patients with NYHA class III and IV heart failure and an EF 25-45%. A total of 160 adult subjects were recruited and have been randomly assigned to either the Optimizer IVs plus OMT, or to a control group receiving OMT alone. One of the exclusion criteria included QRS duration greater than or equal to 130 msec duration. Based on difficulties encountered in reliably quantifying VAT, the relatively large number of studies in which VAT could not be quantified, and the statistical inefficiency and arbitrary nature of thresholds employed in a “responders” analysis of a continuous variable in the FIX-HF-5 study, the primary efficacy end point was changed to compare changes in peak VO2 between the treatment and control groups. This study is registered in ClinicalTrials.gov with an estimated completion date of March 2019 (NCT01381172).

Müller et al. (2017) evaluated clinical effects of long-term CCM in subjects with heart failure (HF) caused by left ventricular systolic dysfunction. Out of 143 subjects from 24 sites, 106 with HFrEF completed the 24 month follow-up which was recorded via a clinical registry. Recordings included NYHA class, MLWHFQ score, 6 min walk distance, LVEF, and peak VO2 at baseline and 6 month intervals as clinically indicated. Serious adverse events, and all cause as well as cardiovascular mortality were recorded. Data are
presented stratified by LVEF (all subjects, LVEF <35%, LVEF ≥35%). The investigators found that baseline parameters were similar among LVEF groups. NYHA and MLWHFQ improved in all 3 groups at each time point. LVEF in the entire cohort improved 2.5, 2.9, 5.0, and 4.9% at 6, 12, 18, and 24 months, respectively. Insufficient numbers of subjects had follow-up data for 6 min walk or peak VO2 assessment, precluding comparative analysis. Serious adverse events (n = 193) were observed in 91 subjects and similarly distributed between groups with LVEF <35% and LVEF ≥35%, and similar to other device trials for heart failure. Eighteen deaths (7 cardiovascularly related) over 2 years. Overall survival at 2 years was 86.4% (95% confidence intervals: 79.3, 91.2%). The investigators concluded that in patients with HFrEF and persistent symptoms despite GDMT, CCM provides sustained improvement in both cardiac function and QOL. The benefit is present not only in subjects with baseline LVEF <35%, but also in those with LVEF ≥35%. These data suggest that CCM may be beneficial in select patients with heart failure, narrow QRS, and symptoms despite optimal medical management. Limitations of the study include: lack of a control group, improvement in NYHA, MLWHFQ, and LVEF could have resulted from the increased use of pharmacological treatment of HF in these patients, and registry follow-up testing was performed based on clinical need, which may have limited the number of patients available with outcomes data related to LVEF and exercise tolerance including 6 min walk test, and peak VO2.

The Optimizer system has been launched in Europe; however, is limited to investigational use
only in the United States (Impulse Dynamics, 2018).

The above policy is based on the following references:


AETNA BETTER HEALTH® OF PENNSYLVANIA

Amendment to
Aetna Clinical Policy Bulletin Number: 0930 Cardiac Contractility Modulation (CCM) Therapy

There are no amendments for Medicaid.

www.aetnabetterhealth.com/pennsylvania  revised 06/01/2018