Medical Coverage Policy

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Cardiac Omnibus Codes

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Related Coverage Resources

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted

for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This Coverage Policy addresses multiple cardiac-related devices and procedures, including:

- Carotid sinus baroreflex activation device (i.e., BAROSTIM™ NEO® System)
- Left Atrial Pressure Sensor (e.g., HeartPOD System, Promote LAP System, V-LAP System)
- Pulmonary artery pressure sensor (e.g., CardioMEMS™ HF system, Cordella™ Pulmonary Artery Sensor System)
- Cardiac contractility modulation (CCM®) therapy (i.e., OPTIMIZER Smart System)
- Inferior vena cava (IVC) sensor (i.e., NORM System by FIRE1)

Coverage Policy

Carotid Sinus Baroreflex Activation Device
Carotid sinus baroreflex activation device (CPT® 0266T, 0268T and HCPCS code C1825) is considered experimental, investigational or unproven.

Left Atrial Pressure Sensor
Implantation and monitoring of a left atrial pressure sensor (CPT® 0933T) is considered experimental, investigational or unproven.

Pulmonary Artery Pressure Sensor
Implantation and monitoring of a pulmonary artery pressure sensor (CPT® 33289 and HCPCS C2624, G0555) is considered experimental, investigational or unproven.

Cardiac Contractility Modulation Therapy
The use of cardiac contractility modulation therapy (CPT® 0408T, 0915T-0918T, 0930T-0931T and HCPCS C1824) is considered experimental, investigational or unproven.

Inferior Vena Cava Sensor
Implantation and monitoring of an inferior vena cava sensor (CPT® 0981T) is considered experimental, investigational or unproven.

Coding Information

Notes:
1. This list of codes may not be all-inclusive since the American Medical Association (AMA) and Centers for Medicare & Medicaid Services (CMS) code updates may occur more frequently than policy updates.
2. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Carotid Sinus Baroreflex Activation Device

Considered Experimental/Investigational/Unproven:

CPT®* Codes	Description
0266T	Implantation or replacement of carotid sinus baroreflex activation device; total system (includes generator placement, unilateral or bilateral lead placement, intra-operative interrogation, programming, and repositioning, when performed)
0268T	Implantation or replacement of carotid sinus baroreflex activation device; pulse generator only (includes intra-operative interrogation, programming, and repositioning, when performed)

HCPCS Codes	Description
C1825	Generator, neurostimulator (implantable), nonrechargeable with carotid sinus baroreceptor stimulation lead(s)

Left Atrial Pressure Sensor

Considered Experimental/Investigational/Unproven:

CPT®* Codes	Description
0933T	Transcatheter implantation of wireless left atrial pressure sensor for long-term left atrial pressure monitoring, including sensor calibration and deployment, right heart catheterization, transseptal puncture, imaging guidance, and radiological supervision and interpretation

Pulmonary Artery Pressure Sensor

Considered Experimental/Investigational/Unproven:

CPT®* Codes	Description
33289	Transcatheter implantation of wireless pulmonary artery pressure sensor for long-term hemodynamic monitoring, including deployment and calibration of the sensor, right heart catheterization, selective pulmonary catheterization, radiological supervision and interpretation, and pulmonary artery angiography, when performed

HCPCS Codes	Description
C2624	Implantable wireless pulmonary artery pressure sensor with delivery catheter, including all system components
G0555	Provision of replacement patient electronics system (e.g., system pillow, handheld reader) for home pulmonary artery pressure monitoring

Cardiac Contractility Modulation Therapy

Considered Experimental/Investigational/Unproven:

CPT®* Codes	Description
0408T	Insertion or replacement of permanent cardiac contractility modulation system, including contractility evaluation when performed, and programming of sensing and therapeutic parameters; pulse generator with transvenous electrodes
0915T	Insertion of permanent cardiac contractility modulation-defibrillation system component(s), including fluoroscopic guidance, and evaluation and programming of sensing and therapeutic parameters; pulse generator and dual transvenous electrodes/leads (pacing and defibrillation)
0916T	Insertion of permanent cardiac contractility modulation-defibrillation system component(s), including fluoroscopic guidance, and evaluation and programming of sensing and therapeutic parameters; pulse generator only
0917T	Insertion of permanent cardiac contractility modulation-defibrillation system component(s), including fluoroscopic guidance, and evaluation and programming of sensing and therapeutic parameters; single transvenous lead (pacing or defibrillation) only
0918T	Insertion of permanent cardiac contractility modulation-defibrillation system component(s), including fluoroscopic guidance, and evaluation and programming of sensing and therapeutic parameters; dual transvenous leads (pacing and defibrillation) only
0930T	Electrophysiologic evaluation of cardiac contractility modulation-defibrillator leads, including defibrillation-threshold evaluation (induction of arrhythmia, evaluation of sensing and therapy for arrhythmia termination), at time of initial implantation or replacement with testing of cardiac contractility modulation-defibrillator pulse generator
0931T	Electrophysiologic evaluation of cardiac contractility modulation-defibrillator leads, including defibrillation-threshold evaluation (induction of arrhythmia, evaluation of sensing and therapy for arrhythmia termination), separate from initial implantation or replacement with testing of cardiac contractility modulation-defibrillator pulse generator

HCPCS Codes	Description
C1824	Generator, cardiac contractility modulation (implantable)

Inferior Vena Cava Sensor

Considered Experimental/Investigational/Unproven:

CPT®* Codes	Description
0981T	Transcatheter implantation of wireless inferior vena cava sensor for long-term hemodynamic monitoring, including deployment of the sensor, radiological supervision and interpretation, right heart catheterization, and inferior vena cava venography, when performed (Do not report 0981T in conjunction with 36010, 36013, 37252, 37253, 75825, 76000, 93451, 93453, 93456, 93460, 93461, 93566, 93593, 93594, 93596, 93597) (For implantation of wireless pulmonary artery sensor, use 33289) (For remote monitoring of an implantable inferior vena cava pressure sensor, use 0982T)

EFFECTIVE 01/15/2026

General Background

CAROTID SINUS BAROREFLEX ACTIVATION DEVICE

Baroreceptors are sensors located in the carotid sinus and in the aortic arch. The carotid sinus baroreceptors are sensitive to pressure changes in the arterial blood pressure and relay the information to the brain. This response brings appropriate changes to maintain heart rate and blood pressure in normal physiological limits, which is known as 'carotid sinus baroreflex'.

Baroreflex activation therapy (BAT) is a device-based approach that consists of an implanted pulse generator (implanted in the pectoral region), external programming system, and leads placed adjacent to the carotid sinus to deliver electrical pulses to the carotid baroreceptors. Electrical stimulation of the carotid baroreceptors results in activation of the baroreflex system.

U.S. Food and Drug Administration (FDA): The BAROSTIM™ NEO® System (CVRx, Inc.) received FDA Premarket Approval Application (PMA) approval on August 16, 2019 (P180050). The BAROSTIM™ NEO® System is indicated for the improvement of symptoms of heart failure – quality of life, six-minute hall walk and functional status, for patients who remain symptomatic despite treatment with guideline-directed medical therapy, are NYHA Class III or Class II (who had a recent history of Class III), have a left ventricular ejection fraction ≤ 35%, a NT-proBNP < 1600 pg/ml and excluding patients indicated for Cardiac Resynchronization Therapy (CRT) according to AHA/ACC/ESC guidelines.

Patients are contraindicated if they have:

- Been assessed to have bilateral carotid bifurcations located above the level of the mandible
- Baroreflex failure or autonomic neuropathy
- Uncontrolled, symptomatic cardiac bradyarrhythmias
- Carotid atherosclerosis that is determined by ultrasound or angiographic evaluation greater than 50%
- Ulcerative plaques in the carotid artery as determined by ultrasound or angiographic evaluation
- Known allergy to silicone or titanium

CVRx received conditional Investigational Device Exemption (IDE) approval from the FDA in October 2006 to begin the Rheos Pivotal Trial. This trial was designed to evaluate the safety and effectiveness of the Rheos Baroreflex Hypertension Therapy System.

Professional Societies/Organizations: The 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure (Heidenreich, et al., 2022) states:

> 7.4.2. Other Implantable Electrical Interventions
> Trials of device stimulation of the vagus nerve, spinal cord, and baroreceptors have had mixed responses.

Literature Review: Wang et al. (2025) retrospectively reported on 23 patients with HFrEF who received BAT at Hannover Medical School between 2014 and 2023. Etiology of heart failure was ischemic in 70%. The majority of patients (96%) suffered from NYHA Class III heart failure. A

complication occurred in one patient during BAT implantation (4%). The mean follow-up was 3 ± 2 (max. 7.5) years. BAT reduced NYHA classification in 12 patients (52%) after 1 year, of which one patient remained in ameliorated NYHA for 7.5 years. Echocardiographic evaluation revealed significant improvement in LVEF by 9 ± 9% after 1 year (P < 0.001) and by 11 ± 9% (P = 0.005) after 2 years. In addition, BAT mildly reduced NT-proBNP in the first 2 years [non-significantly after 1 year by 396 ± 1006 pg/mL and significantly after 2 years by 566 ± 651 pg/mL (P = 0.039)]. Seven patients reaching the recommended replacement time underwent device exchange. Four patients died during observation time.

Blanco et al. (2023) retrospectively reported on 30 patients with chronic heart failure with reduced ejection fraction (HFrEF) who received baroreflex activation therapy (BAT) with the Barostim Neo™ device at a single center in Germany. Most patients (83%) had previous heart failure hospitalization (HFH).

- Median follow-up time for clinical events defined as death or HF hospitalization was 16 (10–33) months. During this time, a total of 10 patients died [2 HF, 3 not related to HF (sepsis, renal failure, and malignancy), and 5 unexplained]. Mortality at 1 and 3 years was 20% and 33.3%.
- A total of 14 patients were hospitalized due to HF during follow-up. One of those patients was hospitalized twice for this reason, resulting in an event rate of 15.
- The LVEF improved from 25.5 (20.0–30.5) % at baseline to 30.0 (25.0–36.0) % at 12 months (*P* = 0.014). NYHA functional class significantly improved between baseline and 12-month follow-up (P < 0.001).
- Limitations of the study include small sample size and retrospective nature of the study.

Coats et al. (2022) conducted an individual patient data (IPD) meta-analysis from all patients enrolled in Abraham et al. (2015) and Zile et al. (2020). A total of 554 randomized patients were included.

- In all patients, BAT provided significant improvement in 6MHW distance of 49m, MLWHF QoL of −13 points, and 3.4 higher odds of improving at least one NYHA class when comparing from baseline to 6 months. These improvements were similar, or better, in patients who had baseline NT-proBNP <1600 pg/ml, regardless of the cardiac resynchronization therapy indication status. NT-proBNP levels appeared to improve in all patients, but only reached statistical significance in the cohorts that excluded patients with NT-proBNP >1600 pg/ml.

The Baroreflex Activation Therapy for Heart Failure trial (BeAT-HF, NCT02627196) (Zile, et al., 2020; Zile, et al., 2024) was a multicenter RCT conducted to the safety and effectiveness of baroreflex activation therapy (BAT) in 408 patients with heart failure with reduced ejection fraction (HFrEF). Patients were randomized to receive either BAT plus optimal medical management (BAT group) or optimal medical management alone (control group).

- The three primary effectiveness endpoints included 6-min hall walk distance (6MHW), Minnesota Living with HF Questionnaire quality-of-life (QOL) score, and N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels. The single safety endpoint was major adverse neurological or cardiovascular system or procedure-related event-free rate (MANCE).
- During the 6-month follow-up, there was a significant difference in medical management between the 2 arms, with a disproportionately higher number of medications added in the control group.
- BAT improved the EuroQol-5 Dimensions (EQ-5D) index by a net difference of Δ=0.10 (p < 0.001). BAT improved NYHA functional class (78 [65%] in the BAT group vs. 39 [31%] in the control group; Δ=34%; p < 0.001) statistically significant).

- Cardiovascular serious adverse events (non-heart failure-related events or non-cardiovascular death) were 0.101 events per patient-year in the BAT group vs. 0.206 in the control group; p= 0.023 (statistically significant); 51% reduction with BAT.
- In the 144 of 408 randomized patients that had a NT-proBNP >1,600 pg/ml, BAT did not have a statistically significant improvement on 6MHW distance or NT-proBNP but did improve QOL score compared with that in the control group.
- The authors concluded that BAT is safe, improved the patient-centered symptomatic endpoints of QOL score, exercise capacity, and functional status, and significantly decreased NTproBNP in patients with NYHA functional class III (or patients with NYHA functional class II who had a recent history of NYHA functional class III), EF ≤35%, NT-proBNP <1,600 pg/ml, and who did not have a Class I indication for CRT.
- Zile et al. (2024) reported analyses that included follow-ups for all BeAT-HF trial patients from randomization until last patient visit. Overall, 323 patients had 332 primary events, with a median of 3.6 years of follow-up/patient. The primary endpoint was a composite of the rate of cardiovascular mortality and HF morbidity. BAT did not result in a significant difference in the composite primary endpoint, CV mortality and HF morbidity, or the individual components of the primary endpoints compared with control.

de Leeuw et al. (2017) analyzed data from all patients who had been included in 1 of the 3 trials that focused on treatment-resistant hypertensive patients. None of the patients had previously undergone another device-based treatment, such as renal denervation. A total of 383 patients were implanted with the first-generation Rheos system (16 in the US Rheos Feasibility Trial, 45 in the DEBuT-HT Trial, and the remainder in the Pivotal Trial). Of the 383 patients available for analysis, 143 patients completed the 5-year follow-up and 48 were followed for 6 years. de Leeuw et al. noted the data reviewed was based on the blood pressure and heart rate responses obtained during 6 years of open follow-up.

- In the entire cohort, office systolic blood pressure fell from 179±24 mm Hg to 144±28 mm Hg (P<0.0001), whereas office diastolic pressure dropped from 103±16 mm Hg to 85±18 mm Hg (P<0.0001). Heart rate fell from 74±15 beats per minute to 71±13 beats per minute (P<0.02). The effect of baroreflex activation therapy is greater than average in patients with signs of heart failure and less than average in patients with isolated systolic hypertension. In approximately 25% of patients, it was possible to reduce the number of medications from a median of 6 to a median of 3.
- The authors stated the most important limitation is the fact that 2 of the 3 studies were nonrandomized, and all lacked a control group during prolonged follow-up. Second limitation is the variable follow-up period. The author s concluded that the analysis has shown that chronic BAT durably lowers blood pressure in treatment-resistant hypertensive patients. It is markedly effective when hypertension is complicated by heart failure with preserved ejection fraction. Altogether, these results justify further development and implementation of device-based therapy for resistant hypertension and heart failure, including those with reduced ejection fraction.

In a multinational RCT (HOPE4HF), Abraham et al. (2015) assessed the safety and efficacy of carotid baroreflex activation therapy (BAT) in advanced HF.

- Patients with New York Heart Association (NYHA) functional class III HF and ejection fractions ≤35% on chronic stable guideline-directed medical therapy (GDMT) were enrolled at 45 centers in the United States, Canada, and Europe. They were randomly assigned to receive ongoing GDMT alone (control group) or ongoing GDMT plus BAT (treatment group) for 6 months. The primary safety end point was system- and procedure-related major adverse neurological and cardiovascular events. The primary efficacy end points were changes in NYHA functional class, quality-of-life score, and 6-minute hall walk distance.

- Of the 69 patients assigned to the control group who reached their activation dates, 15 did not complete 6 months of follow-up: 4 patients died, 5 withdrew consent, 3 were lost to follow-up, and 3 missed the visit.
- Of the 71 patients who received the BAT system and reached their activation date, 7 did not complete 6 months of follow-up: 5 died and 2 withdrew consent. At 6 months, statistically significant improvements were observed in NYHA functional class, MLWHFQ QoL score, and 6MHW distance in BAT patients compared with control patients ($p = 0.002$, $p < 0.001$, and $p = 0.004$, respectively). NT-proBNP was reduced in the treatment group and increased in the control group, with a significant between-group difference ($p=0.02$).
- Weaver et al. (2016) reported on a total of 101 HOPE4HF trial patients who completed 12 months of follow-up (57 BAT+GDMT, 44 GDMT). Significant beneficial treatment effects in SBP, NT-proBNP, 6MHW, QOL, and NYHA Class observed at 6 months were sustained through 12 months, both for the study population as a whole as well as the no-CRT cohort. In the no-CRT cohort, improvement in NYHA Class for BAT+GDMT reached statistical significance, a finding not observed in the 6-month analysis.

Zile et al. (2015) conducted a study to define the differences in treatment effect produced by BAT in two protocol prespecified groups of patients: those with vs. those without cardiac resynchronization therapy (CRT) present. Some data was collected retrospectively, some prospectively.

- NYHA Class III chronic HF patients with an LVEF ≤35% were randomized to receive ongoing GDMT alone (control group) or ongoing GDMT plus BAT (BAT group).
- The CRT vs. no-CRT groups were similar with respect to baseline characteristics, except for the following characteristics: the no-CRT patients were younger, more frequently had hypertension noted in their medical history, and had a shorter QRS.
- Of the 69 patients assigned to the control group who reached their activation date, 21 had a CRT, 48 did not have a CRT. In the CRT control group patients, four did not complete 6 months of follow-up: two patients died, one withdrew consent, and one missed the visit. In the no-CRT control group patients 11 did not complete 6 months of follow-up: two patients died, four withdrew consent, three were lost to follow-up, and two missed the visit.
- Of the 71 patients implanted with the BAT system reaching their activation date 24 had a CRT and 47 did not. In the CRT BAT group patients two did not complete 6 months of follow-up (owing to death). In the no-CRT BAT group patients, five did not complete 6 months of follow-up: three patients died and two withdrew consent.
- MANCE-free rate at 6 months was 100% in CRT and 96% in no-CRT group. The difference was statistically significant in QoL score ($P = 0.04$), 6MHWD ($P = 0.01$), and LVEF ($P=0.02$), marginally significant in NYHA and HF hospitalization days, and not significant in NT proBNP and number of HF hospitalizations. Limitations of this study include small sample size and retrospective data collection.

LEFT ATRIAL PRESSURE (LAP) SENSOR

Approximately 90% of patients admitted to the hospital for heart failure have pulmonary congestion related to elevated left atrial filling pressure. Intracardiac remote pressure monitoring devices are proposed to reduce HF hospitalizations and an improvement in quality of life.

U.S. Food and Drug Administration (FDA): It remains unclear if these devices are available for use in the United States and/or FDA-approved:

- HeartPOD System (Abbott)
- Promote LAP System (Abbott)

- V-LAP System (Vectorious Medical Technologies, Israel) A cardiac news website states that the FDA granted Vectorious Medical Technologies Ltd a breakthrough device designation for left atrial pressure sensor, V-LAP, for heart failure in December 2020.

Professional Societies/Organizations: The 2017 Heart Failure Society of America (HFSA) Scientific Statements Committee White Paper on Remote Monitoring of Patients With Heart Failure (Dickenson, 2018) discusses the Left Atrial Pressure Monitoring to Optimize Heart Failure Therapy (LAPTOP-HF) trial.

- It was a multicenter, randomized, controlled clinical trial in ambulatory patients with advanced heart failure. It was planned to enroll up to 730 patients with New York Heart Association functional class III symptoms and either a hospitalization for HF during the previous 12 months or an elevated B-type natriuretic peptide level, regardless of ejection fraction, at up to 75 investigational centers. Randomization to the treatment group or control group will be at a 1:1 ratio in 3 strata based on the ejection fraction (EF>or ≤35%) and the presence of a de novo CRT device indication.
- Two implantable LAP monitoring systems were to be used depending on clinical indications and the implanter's discretion, HeartPOD and, if cardiac resynchronization therapy (CRT) is indicated and the implanting physician chooses to place a single device, a Promote CRT-D LAP pulse generator that accommodates 3 pacing/defibrillating leads and the HeartPOD implantable sensor lead (ISL).
- Dickenson et al. notes that the LAPTOP-HF trial was terminated after 486 patients were enrolled owing to a cluster of implant-related complications. From the available data presented, the trial suggested that the hemodynamic monitoring and associated management algorithm for patient-directed therapy adjustments could have been effective.

The 2022 American College of Cardiology/ American Heart Association/ Heart Failure Society of America (ACC/AHA/HFSA) guideline for the Management of Heart Failure does not address use of implantable left atrial pressure devices (Heidenreich, 2022).

Literature Review: D'Amario et al. (2023), Perl et al. (2022) and Meerkin et al. (2024) reported on the V-LAP Left Atrium Monitoring systEm for Patients With Chronic sysTOlic & Diastolic Congestive heart Failure (VECTOR-HF) study, a prospective, multicenter, single-arm, open-label clinical trial.

- The miniaturized V-LAP™ system device was successfully implanted in all 30 patients and enrolled NYHA functional class III HF patients, who were already in guideline-directed optimal medical and device therapy, irrespectively of left ventricular ejection fraction (LVEF).
- After 3 months, a right heart catheterization was performed to correlate mean pulmonary capillary wedge pressure (PCWP) with simultaneous mean LAP obtained from the device (27 out of 30). Remote LAP measurements were then used to guide patient management.
- At 3 months, the mean difference between left atrial pressure (LAP) and PCWP was −0.22±4.92 mmHg. To date, with a mean follow-up period of 22 months, there are a total of 52 serious adverse events (SAEs), out of which only one was considered possibly device-related (CVA). Four patients passed away during follow-up and were determined as unlikely (n=1) or not related (n=3) to the study device.
- The authors concluded that preliminary clinical results are encouraging, supporting a possible leading role for left-sided pressure-guided management in patients with HF. Further studies are needed to confirm the long-term safety and performance of the V-LAP device in patients with HF and, importantly, powered enough to test the efficacy of this strategy when compared to the current standard of care in preventing HF-related rehospitalization and major adverse cardiac events.

- Meerkin et al. (2024) reported interim results of 13 patients (from the VECTOR-HF I and IIa studies). Over 12 months, no procedure- or device-related major adverse cardiovascular or neurological events were observed, and there were no failures to obtain measurements from the sensor and transmit the data to the HCP interface and the patient guidance application. Patient adherence was 91.4%.

Ritzema et al. (2010) conducted a prospective, observational HeartPOD HOMEOSTASIS trial comprised the first 20 patients enrolled in 3 Australian/New Zealand sites and the first 20 patients enrolled in 4 US centers (total 40).

- Patients were eligible if they had a history of New York Heart Association class III or ambulatory class IV heart failure of at least 6 months, regardless of left ventricular ejection fraction. They were required to have at least 1 episode of acute decompensated heart failure treated with intravenous therapy during the prior year and to be taking maximally tolerated, stable doses of an angiotensin-converting enzyme (ACE) inhibitor or angiotensin-receptor blocker (ARB) and a β-blocker if left ventricular ejection fraction was <40%.
- Readings were acquired twice daily. For the first 3 months, patients and clinicians were blinded as to these readings, and treatment continued per usual clinical assessment. Thereafter, left atrial pressure and individualized therapy instructions guided by these pressures were disclosed to the patient.
- A median follow-up of 25 months (range 3 to 38 months) was available in 39 patients (97.5%). There were 22 episodes of acute decompensated heart failure that required intravenous treatment. Altogether, 15 patients had 28 events. Event-free survival was 0.72 at 1 year, 0.69 at 2 years, and 0.61 after 3 years.
- The authors concluded that physician-directed patient self-management of heart failure with direct LAP monitoring was associated with improved LAP control, reduced symptoms, more optimal neurohormonal antagonist and diuretic dosing, and a reduction of early clinical events.

Ritzema et al. (2007) reported on the Hemodynamically Guided Home Self-Therapy in Severe Heart Failure Patients (HOMEOSTASIS I) trial, a single center, prospective feasibility trial of the permanently implantable LAP monitoring system (HeartPOD) in eight (8) ambulatory patients with class III to IV HF and at least 1 hospital admission or presentation to an emergency department or clinic for acute decompensated HF requiring parenteral diuretic, vasodilator, or positive inotrope during the previous 12 months.

- At the 12-week follow-up, 87% of device LAP measurements were within ±5 mm Hg of simultaneous pulmonary capillary wedge pressure readings over a wide range of pressures (1.6 to 71 mm Hg). The authors concluded that the new implantable device was well tolerated, feasible, and accurate at a short-term follow-up.

PULMONARY ARTERY PRESSURE SENSOR

Heart failure (HF) is a complex clinical syndrome identified by presence of current or prior characteristic symptoms, such as dyspnea and fatigue, and evidence of cardiac dysfunction as a cause of these symptoms (e.g., abnormal left ventricular [LV] and/or right ventricular [RV] filling and elevated filling pressures). The functional status of patients with HF is often described using the New York Heart Association (NYHA). The NYHA classification, with severity of disability ranging from I to IV is the classification system that is most commonly used to quantify the degree of functional limitation imposed by HF is one first developed by the NYHA. This system assigns patients to one of four functional classes, depending on the degree of effort needed to elicit symptoms:

- Class I – Patients with heart disease without resulting limitation of physical activity. Ordinary physical activity does not cause HF symptoms such as fatigue or dyspnea.

- Class II – Patients with heart disease resulting in slight limitation of physical activity. Symptoms of HF develop with ordinary activity but there are no symptoms at rest.
- Class III – Patients with heart disease resulting in marked limitation of physical activity. Symptoms of HF develop with less than ordinary physical activity but there are no symptoms at rest.
- Class IV – Patients with heart disease resulting in inability to carry on any physical activity without discomfort. Symptoms of HF may occur even at rest.

Methods for obtaining pulmonary artery pressure (PAP) in patients with chronic heart failure include a right heart catheterization (RHC) procedure or PAP monitoring with an implantable hemodynamic monitoring system which also gets implanted via a RHC. A RHC is a procedure during which a catheter is inserted through a large vein in the neck or groin and subsequently advanced into the pulmonary artery. There are significant risks in undergoing a RHC, whether for repeated direct measurements or for the implantation of a PAP monitoring medical device.

U.S. Food and Drug Administration (FDA): The CardioMEMS™ HF system received FDA approval on May 28, 2014 (Abbotts, formerly St. Jude Medical, Inc., St. Paul, MN) (PMA P100045). The CardioMEMS HF System includes the CM2000 implantable PA Sensor/Monitor and transvenous catheter delivery system, the CM1000 Patient Electronics System (GSM), the CM1010 Patient Electronics System (GSM), and CM3000 Hospital Electronics System.

- According to the PMA, the device is indicated for wirelessly measuring and monitoring pulmonary artery (PA) pressure and heart rate in patients with New York Heart Association (NYHA) Class III HF who have been hospitalized for HF in the previous year.
- In February 2022, the FDA approved a PMA supplement for the CardioMEMs HF System (St. Jude Medical [Abbott]) for expanding the indications to include NYHA Class II patients (P100045/S056). The Feb 18, 2022 approval letter states: "The CardioMEMS HF System is indicated for wirelessly measuring and monitoring pulmonary artery pressure and heart rate in NYHA Class II or III heart failure patients who either have been hospitalized for heart failure in the previous year and/or have elevated natriuretic peptides. The hemodynamic data are used by physicians for heart failure management with the goal of controlling pulmonary artery pressures and reducing heart failure hospitalizations."

The Cordella™ Pulmonary Artery Sensor System (CorPASS) (Endotronix, Inc.) received FDA PMA approval on 06/20/2024 (P230040).

- Indications for Use: The Cordella Pulmonary Artery Sensor System is intended to measure, record and transmit pulmonary artery pressure (PAP) data from NYHA Class III heart failure patients who are at home on diuretics and guideline-directed medical therapy (GDMT) as well as have been stable for 30 days on GDMT. The device output is meant to aid clinicians in the assessment and management of heart failure, with the goal of reducing heart failure hospitalizations.
- Contraindications: The Cordella Pulmonary Artery Sensor System is contraindicated for patients with an inability to take dual antiplatelet or anticoagulants for one month post implant.
- Device description: The Cordella PA Sensor System is designed to be used with the Cordella Heart Failure System to better connect healthcare professionals and patients with tools for heart failure management. The Cordella PA Sensor is an implantable blood pressure monitor that permanently resides in the patient's pulmonary artery. With this Sensor, PA pressure can be wirelessly measured from the patient's home on demand. Active management of a patient using PA pressure data from the Cordella Sensor and vital signs and patient-reported symptoms data from Cordella HF System may improve long-

term outcomes in patients with NYHA Class III heart failure. The Cordella PA Sensor System is comprised of the following subsystems:

- Cordella PA Sensor
- Cordella Delivery System
- myCordella Handheld Patient Reader (including Dock)
- Cordella Calibration Equipment (CalEQ)
- Cordella Data Analysis Platform (CDAP)

Professional Societies/Organizations: The ACC/AHA/Heart Failure Society of America (HFSA) 2022 Guideline for the Management of Heart Failure Section 4.6. Wearables and Remote Monitoring (Including Telemonitoring and Device Monitoring), notes the following:

- In selected adult patients with NYHA class III HF and history of a HF hospitalization in the past year or elevated natriuretic peptide levels, on maximally tolerated stable doses of GDMT with optimal device therapy, the usefulness of wireless monitoring of PA pressure by an implanted hemodynamic monitor to reduce the risk of subsequent HF hospitalizations is uncertain (2b B-R*).
- In patients with NYHA class III HF with a HF hospitalization within the previous year, wireless monitoring of the PA pressure by an implanted hemodynamic monitor provides uncertain value. (Value Statement: Uncertain Value, B-NR) (Heidenreich, et al., 2022).
  *See Appendix for ACC/AHA Class of Recommendation and Level of Evidence

A 2023 Journal of the American College of Cardiology (JACC) Scientific Statement on Remote Monitoring for Heart Failure Management at Home (Stevenson, et al., 2023) summarized "To manage HF at home, signals need to be accurate and actionable, with response kinetics for early relooks after intervention. The major target for decreasing HFH and improving quality of life is relief and prevention of congestion, for which tracking of cardiac filling pressures or lung water content has shown most benefit thus far. Algorithms need to be personalized with more precision for signal thresholds and for levels of intervention, some of which should be automated for direct patient access. For patients at lower risk of HF events, multiparameter scores from implanted rhythm devices have identified patient trends for which clinical evaluation may be warranted." Highlights:

- Remote monitoring coupled with a system of care that engages, informs, and empowers patients is essential for effective home management of HF to control symptoms, avoid hospitalization, and ameliorate the patient's perception of illness.
- Effective remote monitoring requires an accurate, reliable signal that is actionable through personalized algorithms.
- Evolving digital health care must address the digital divide and deep gaps in access to HF management (Stevenson, et al., 2023).

Literature Review: Following GUIDE-HF (Hemodynamic-GUIDEd Management of Heart Failure Trial), with U.S. Food and Drug Administration input, PROACTIVE-HF (A Prospective, Multi-Center, Open Label, Single Arm Clinical Trial Evaluating the Safety and Efficacy of the Cordella Pulmonary Artery Sensor System in NYHA Class III Heart Failure Patients trial) was changed from a randomized to a single-arm, open label trial, conducted at 75 centers in the USA and Europe. The purpose of the study was to evaluate the effect of managing seated mean pulmonary artery pressure (mPAP) with the Cordella Pulmonary Artery sensor on outcomes in patients with HF.

- Inclusion criteria included: men or women >18 years of age with a diagnosis and treatment of HF (regardless of left ventricular ejection fraction [LVEF]) for at least 3 months and NYHA functional class III symptoms at the time of screening. Patients were to be on stable, optimally titrated guideline-directed medical therapy (GDMT) for at least 30 days before screening. Patients had to have at least 1 HF hospitalization, HF treatment in a hospital

day-care setting, or urgent outpatient clinic HF visit within 12 months and/or elevated N-terminal prohormone of brain natriuretic peptide (NT-proBNP). The primary effectiveness endpoint at 6 months required the HF hospitalization or all-cause mortality rate to be lower than a performance goal of 0.43 events/patient, established from previous hemodynamic monitoring trials.

- Between December 2019 and March 2023, 738 patients were screened with 125 screening failures. Before the change to single arm, 72 patients were randomized to the former control arm. There were 48 withdrawals before the implant, leaving 493 patients in the intent-to-treat population (safety analysis), and there were 37 aborted implants (Supplemental Methods), leaving 456 patients in the modified intent-to-treat population (primary cohort). This population was comprised of the former treatment arm (n=88) and newly enrolled single arm (n=368).
- The 6-month event rate was 0.15 which was significantly lower than performance goal (0.15 vs 0.43; P < 0.0001). Freedom from device- or system-related complications was 99.2% and freedom from sensor failure was 99.8% through 6 months. The authors concluded that results support the use of seated mPAP monitoring and extend the growing body of evidence that pulmonary artery pressure–guided management improves outcomes in heart failure (Guichard, et al., 2024).

The CardioMEMS HF System Post-Market Study (COAST) was a French, prospective open-label cohort study including 103 NYHA class III patients with at least one heart failure hospitalization in the 12 months before enrollment, regardless of left ventricular ejection fraction. The primary efficacy endpoint was evaluated comparing the rate of heart failure hospitalization during the year before and the year after implantation. There were 179 heart failure hospitalizations in the year before implantation compared with 79 in the year after implantation (risk reduction 50.3%; rate ratio 0.50, 95% confidence interval 0.38-0.66; P<0.0001). During the 2 years of follow-up, pulmonary artery pressures were lowered significantly (mean pulmonary artery pressure -3.7±6.3mmHg; P<0.0001), with a significant improvement in functional class and quality of life. The authors stated that their results demonstrate that implantation of CardioMEMS™ is safe, and that the system is reliable, with no device/system-related complications or pressure sensor failures up to 24 months after implantation (de Groote, et al., 2024). **LoE: 3**

Sharif et al. (2024) conducted a prospective, multi-centre, open-label, single-arm trial (SIRONA 2) evaluating the safety and efficacy of the Cordella PAP sensor and Cordella HF system in NYHA class III HF patients in Europe with HF hospitalizations (HFH) and/or an increase in natriuretic peptides in the previous 12 months. The primary efficacy endpoint was the accuracy of the PA sensor mean PAP (mPAP) measurement compared with the fluid-filled catheter during right heart catheterization (RHC) at 90 days.

- Inclusion criteria: Participants included were men or women over 18 years of age with a diagnosis of NYHA class III HF with reduced ejection fraction (HFrEF) or HF with preserved ejection fraction (HFpEF) for at least 6 months treated for a minimum of 3 months and stable for at least 1 month prior to enrolment. Patients had to have at least one HF-related hospitalization, HF treatment in a hospital day-care setting, or unplanned outpatient clinic HF visit within 12 months prior to consent and/or increase of brain natriuretic peptide (BNP) or N-terminal pro-BNP at time of screening. Twenty-two (31.4%) had a preexisting implantable cardioverter-defibrillator device, and 13 (18.6%) had a cardiac resynchronization therapy (CRT) or CRT-defibrillator device. Twenty (28.6%) patients had left ventricular ejection fraction (LVEF) ≥ 50%.
- Results: A total of 70 patients were implanted with the Cordella PA Sensor System, 68 who were still in the study 12 months post-implant.

  - PAP sensor accuracy at the 12 month follow-up visit was assessed in 48 of the 70 implanted subjects via concurrent Cordella and fluid-filled RHC measurements. Tests of PA sensor accuracy indicated agreement between Cordella PA Sensor System and RHC PAP measurements at 12 months.
  - Fourteen patients (20.0%) experienced 18 HFH events (defined as in-hospital, hospital day-care setting, or urgent outpatient clinic HF visits) through 12 months. This translated into an event per patient year (EPPY) of 0.27. When examining the composite HFH plus death (N = 5 deaths), there were 23 events with an 0.33 EPPY.
- Study limitations: First, the major methodological limitation is the lack of a control group under standard HF care management. Second, comparison between HFHs prior to sensor implant and after sensor implant may be affected by a lack of robust study definition of HFH prior to sensor implant. Finally, nine months after SIRONA 2 began enrolment, the COVID-19 pandemic began.
- Author conclusion: Cordella wireless implantable PAP sensor system, incorporating comprehensive vital signs and PAP monitoring, along with high levels of patient engagement, enables long-term safe and accurate monitoring of HF status in NYHA class III HF patients (Sharif, et al., 2024).

Urban et al. (2024) conducted a meta-analysis examining the efficacy of pulmonary artery pressure (PAP) monitoring devices (CardioMEMS and Chronicle [not FDA-approved]) in preventing adverse outcomes in HF patients, addressing gaps in prior randomized controlled trials (RCTs). Five RCTs (2572 participants) were systematically reviewed.

- PAP monitoring significantly reduced HF-related hospitalizations ($p = 0.0006$) and HF events ($p = 0.03$), with no impact on all-cause or cardiovascular mortality. The risk of bias was generally high, with evidence certainty ranging from low to moderate. PAP monitoring devices exhibit promise in diminishing HF hospitalizations and events, especially in CardioMEMS and blinded studies. However, their influence on mortality remains inconclusive.
- Further research, considering diverse patient populations and intervention strategies with extended follow-up, is crucial for elucidating the optimal role of PAP monitoring in HF management.

Brugts et al. (2023) conducted an open-label, randomized trial (MONITOR-HF) done in 25 centers in the Netherlands. A total of 348 patients with chronic heart failure of New York Heart Association class III and a previous heart failure hospitalization were randomly assigned to:

1. CardioMEMS-HF group (n=176) (heart failure management with guideline-directed medical therapy [GDMT] and diuretics with the addition of hemodynamic monitoring by a pulmonary artery pressure sensor); or
2. standard care group (n=172) (heart failure management with GDMT and diuretics).

CardioMEMS-HF participants:

- Of the 176, 168 received treatment (8 did not receive intervention because 5 withdrew informed consent, 1 met exclusion criteria, 2 died before implantation).
- Of the 168, 49 discontinued treatments (7 withdrew informed consent, 40 died, and 2 stopped active monitoring [1 non-compliance, 1 sensor failure]).
- 176 included in intention-to-treat (ITT) analysis

Standard care participants:

- 172 received treatment
- 50 discontinued treatments (5 withdrew informed consent, and 45 died)
- 172 included in intention-to-treat (ITT) analysis

The primary endpoint was the mean difference in the Kansas City Cardiomyopathy Questionnaire (KCCQ) overall summary score at 12 months. The mean follow-up time was 1.8 years.

- The mean change in KCCQ overall summary scores between baseline and 12 months among patients in the CardioMEMS-HF group was +7.05 (p=0.0014), compared with -0.08 points among those in the standard care group (p=0.97).
- The total number of heart failure hospitalizations was 117 in the CardioMEMS-HF group and 212 in the control group.
- The median NT-proBNP was significantly reduced from 2377 pg/mL at baseline to 1708 pg/mL (p=0.013) at 12 months in the CardioMEMS-HF group. In the standard care group, there was non-significant difference in NT-proBNP (1907 pg/mL to 1607 pg/mL, p=0.81) at 12 months.

There was no difference on CV/all-cause mortality in patients with CardioMEMS or standard of care. The authors summarized that this MONITOR-HF study showed that hemodynamic monitoring and subsequent individualized adjustment of diuretics and GDMT significantly improved QOL and reduced the number of heart failure hospitalizations. The authors noted a study limitation is the open-label design, as well as the absence of a device (or sham) in controls, which can be prone to bias in the QOL endpoint by unmasking. Another study limitation is the large percentage of treatments that were discontinued, in both groups, for various reasons including death.

The hemodynamic-GUIDEed management of Heart Failure trial (GUIDE-HF) included a randomized arm (n=1000, completed) and a single-arm, observational study (n=2600, ongoing) (Lindenfeld, et al., 2019; Lindenfeld, et al., 2021; Zile, et al., 2022). The single arm of the trial is an observational arm in which NYHA class III patients (n = 2,600) with either a previous heart failure hospitalization (HFH) or elevated natriuretic peptides (but no recent HFH) will be implanted with a PA pressure sensor and observed for occurrence of the primary composite end point of cumulative HF events and mortality at 12 months.

- The randomized arm was a multicenter, single-blind study at 118 centers in the USA and Canada. The study enrolled 1022 patients with NYHA functional class II–IV heart failure, regardless of left ventricular ejection fraction, with a heart failure hospitalization within the 12 months before study consent or elevated natriuretic peptides (B-type natriuretic peptide [BNP] or N-terminal pro-BNP [NT-proBNP]) within 30 days before study consent. A total of 22 patients had unsuccessful implants. This left 1000 participants receiving an implantable PA pressure sensor (CardioMEMS HF System) who were then randomly assigned (1:1) to either hemodynamic-guided heart failure management based on pulmonary artery pressure (n=497) or a usual care (control) group (n=503). Patients were masked to their study group assignment. Investigators were aware of treatment assignment but did not have access to pulmonary artery pressure data for control patients. The primary study end point is the composite of cumulative HF events and all-cause mortality at 12 months. Secondary end points include quality-of-life and functional assessments. A total of 25 treatment group patients and 44 control group patients withdrew from the study before 12 months.
- The authors reported that hemodynamic-guided management did not reduce the combined endpoint of all-cause mortality, heart failure hospitalizations, and urgent heart failure hospital visits despite significant reductions in pulmonary artery pressure during study follow-up compared with the control group. They found no significant between-group differences in the prespecified secondary endpoints of total heart failure events, health related quality of life (KCCQ-12 and EQ-5D-5L), or functional capacity (6MHW). The authors stated that the COVID-19 pandemic had an important effect on the trial. A pre-COVID-19 impact analysis indicated a possible benefit of hemodynamic-guided management on the primary outcome in the pre-COVID-19 period, primarily driven by a lower heart failure hospitalization rate compared with the control group (Lindenfeld, et al., 2019; Lindenfeld, et al., 2021).
- Zile et al. (2022) noted that the authors sought to evaluate the effect of LVEF on treatment outcomes in the GUIDE-HF trial. Zile et al. reported there were 177 primary events

(0.553/patient-year) in the treatment group and 224 events (0.682/patient-year) in the control group (P=0.049); HF hospitalization was lower in the treatment vs control group (P=0.0072). Within each EF subgroup, primary endpoint and HF hospitalization rates were lower in the treatment group (HR <1.0 across the EF spectrum). Event rate reduction by EF in the treatment groups was correlated with reduction in pulmonary artery pressures and medication changes.

Shavelle et al. (2020) conducted a multi-center, prospective, open-label, observational, single-arm trial to assess the efficacy and safety of PA pressure-guided therapy in routine clinical practice with special focus on subgroups defined by sex, race, and ejection fraction (one-year outcomes from the CardioMEMS Post-Approval Study [PAS]).

- The study included 1,200 patients with New York Heart Association class III heart failure (HF) and a prior heart failure hospitalization (HFH) within 12 months and evaluated patients undergoing PA pressure sensor implantation between September 1, 2014, and October 11, 2017. The primary efficacy outcome was the difference between rates of adjudicated HFH one year after compared with the one year before sensor implantation. Safety end points were freedom from device- or system-related complications at two years and freedom from pressure sensor failure at two years. The mean age was 69 years, 37.7% were women, 17.2% were non-White, and 46.8% had preserved ejection fraction (37.7% women; Black 14.3%; Asian 1%; Other 1.5%).
- For the duration of year after sensor implantation, the mean rate of daily pressure transmission was 76±24% and PA pressures declined significantly. The rate of HFH was significantly lower at one year compared with the year before implantation (P<0.0001). The rate of all-cause hospitalization was also lower following sensor implantation (P<0.0001). Results were consistent across subgroups defined by ejection fraction, sex, race, cause of cardiomyopathy, presence/absence of implantable cardiac defibrillator or cardiac resynchronization therapy and ejection fraction. Freedom from device- or system-related complications was 99.6%, and freedom from pressure sensor failure was 99.9% at 1 year. The authors found that both HF hospitalizations and all-cause hospitalizations were significantly lower in the year following implantation of a PA pressure sensor to guide HF management. The magnitude of decrease in PA pressures was related to baseline PA pressures, with greatest reductions in those with the highest pressures at baseline. Reductions in HF hospitalization were consistent across sex and race, across all EF ranges and in addition to best medical and rhythm device therapy.

DeFilippis et al. (2021) reported on a cohort of the above CardioMEMS Post-Approval Study (PAS) study (Shavelle, et al., 2020) to examine sex differences in response to ambulatory hemodynamic monitoring in clinical practice. Four hundred fifty-two women (38% of total) enrolled in the PAS were less likely to be White (78% versus 86%) and more likely to have non-ischemic cardiomyopathy (44% versus 34%) and had significantly higher systolic blood pressure (132 versus 124 mm Hg), mean ejection fraction (44% versus 36%), and pulmonary vascular resistance (3.2 versus 2.6 WU) than men (P<0.001 for all). Both sexes experienced significant decreases in heart failure hospitalizations (HFH) over 12 months. In adjusted models, there were no significant differences in change in HFH between men and women (interaction P=0.13) or all-cause mortality at one year.

Angermann et al. (2020) reported on a prospective, non-randomized, multicenter study (CardioMEMS European Monitoring Study for Heart Failure [MEMS-HF]) to evaluate the safety, feasibility, and performance of CardioMEMS™ HF system in Germany, The Netherlands, and Ireland. The study noted that previously, the findings have not been replicated in health systems outside the United States.

- The study included 234 NYHA class III patients (68 ± 11 years, 22% female, ≥1 HFH in the preceding year) from 31 centers that were implanted with a CardioMEMS sensor and underwent pulmonary artery pressure (PAP)-guided heart failure (HF) management.
- The co-primary outcomes were one-year rates of freedom from device- or system-related complications and from sensor failure and the results were 98.3% [95% confidence interval (CI) 95.8-100.0] and 99.6% (95% CI 97.6-100.0), respectively. Survival rate was 86.2%.
- The secondary endpoints was annualized HFH rate during 12 months after vs.12 months before implant and additional endpoints included: 12-month all-cause death rate; PAP change from baseline; changes in the KCCQ clinical and overall summary scores (CSS, OSS), 20 PHQ-9 sum score, 21 and EQ-VAS score 22 at six and 12 months; changes in HF medications and NYHA class at six and 12months; patient compliance with taking PAP readings, and healthcare provider compliance for weekly PAP readings.
- For the 12 months post- vs. pre-implant, HF hospitalizations (HFH) decreased by 62% (0.60 vs. 1.55 events/patient-year; hazard ratio 0.38, 95% CI 0.31-0.48; P < 0.0001). After 12 months, mean PAP decreased by 5.1 ± 7.4 mmHg, Kansas City Cardiomyopathy Questionnaire (KCCQ) overall/clinical summary scores increased (P < 0.0001), and the 9-item Patient Health Questionnaire sum score improved (P < 0.0001). The study is limited by the lack of randomization, and a control group, and use of within-patient comparisons.

Abraham et al. (2016) examined the results of the above CHAMPION study (Abraham, et al., 2011) over 18 months of randomized follow-up and the clinical effect of open access to pressure information for an additional 13 months in patients formerly in the control group.

- The primary outcome was the rate of hospital admissions between the treatment group and control group in both the randomized access and open access periods. Analyses were by intention to treat. The study included 550 patients that were randomly assigned to either the treatment group (n=270) or to the control group (n=280). 347 patients (177 in the former treatment group and 170 in the former control group) completed the randomized access period and transitioned to the open access period.
- Over the randomized access period, rates of admissions to hospital for heart failure were reduced in the treatment group by 33% (hazard ratio [HR] 0·67 [95% CI 0·55-0·80]; p<0·0001) compared with the control group. After pulmonary artery pressure information became available to guide therapy during open access (mean 13 months), rates of admissions to hospital for heart failure in the former control group were reduced by 48% (HR 0·52 [95% CI 0·40-0·69]; p<0·0001) compared with rates of admissions in the control group during randomized access. Eight (1%) device-related or system related complications and seven (1%) procedure-related adverse events were reported.
- The reduction in the need for admission to hospital, both all-cause and heart failure related, seen during the first six months was maintained during longer randomized access follow-up and subsequently during open access in which adjustment of therapy was no longer monitored by study staff protocol.

In a subgroup analysis of the CHAMPION trial, Krahnke et al. (2015) compared HF and respiratory hospitalization rates in the entire CHAMPION cohort with the rates observed within the COPD and non-COPD subgroups. A total of 187 subjects met criteria for classification into the COPD subgroup.

- In the entire cohort, the treatment group had a 37% reduction in HF hospitalization rates (P<.0001) and a 49% reduction in respiratory hospitalization rates (P=.0061). In the COPD subgroup, the treatment group had a 41% reduction in HF hospitalization rates (P=.0009) and a 62% reduction in respiratory hospitalization rates (P=.0023). The rate of respiratory hospitalizations in subjects without COPD was not statistically different (P=.76).

- The authors stated that HF management incorporating hemodynamic information from an implantable PA pressure monitor significantly reduces HF and respiratory hospitalizations in HF subjects with comorbid COPD compared with standard care. The authors noted a limitation of this study was that pulmonary function test data were not available in this study and were not part of the COPD classification criteria.

Abraham et al. (2011) reported results of a randomized controlled trial (RCT): the CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA Class III Heart Failure Patients (CHAMPION) trial. The outcomes of this trial were reviewed by the FDA for premarket approval of this device.

- Eligible patients underwent implantation of a wireless pulmonary artery (PA) sensor monitoring system (i.e., CardioMEMS). Five hundred fifty individuals were implanted and randomized to the treatment group (n=270, standard of care HF treatment, plus PA pressure readings) or to the control group (n=280), standard of care HF treatment). Daily PA pressure readings were taken at home by patients in each group and sent to a secure website. In the treatment group clinicians had access to these readings; in the control group clinicians were unable to access pressure readings. Assessment at one, three and six months, and every six-months thereafter included a physical examination, assessment of New York Heart Association class and quality-of-life assessment by use of the 21-question Minnesota Living with Heart Failure questionnaire and review of drugs.
- The primary efficacy endpoint was the rate of heart failure-related hospitalizations during the six months after insertion of the pressure sensor in the treatment group versus the control group. The two primary safety endpoints were device-related or system-related complications. The mean follow-up was 15 months.
- At six months 83 heart-failure-related hospitalizations were reported in the treatment group compared with 120 in the control group ($p<0.0001$). During the entire follow-up (mean 15 months) the treatment group had a 39% reduction in heart-failure-related hospitalization compared with the control group ($p<0.0001$). Eight patients had device- or system-related complications (DSRC). Overall freedom from DSRC was 98.6%. Overall freedom from pressure-sensor failures was 100%. Survival rates in the treatment and control groups at six months were similar ($p=0·45$). Fifteen serious adverse events (AE) were reported, including, infection, bleeding, thrombosis, cardiac arrhythmias, one patient with cardiogenic shock, one atypical chest pain, and one delivery-system failure that required a snare to remove the delivery system.
- Data in this single clinical trial suggest improved short-term outcomes; however, additional large blinded RCTs replicating these findings are required before use of a wireless pulmonary artery sensor monitoring system (e.g., CardioMEMS HF system) is incorporated into routine clinical practice.

CARDIAC CONTRACTILITY MODULATION THERAPY

CCM® is the brand name for cardiac contractility modulation (CCM), the non-excitatory electrical pulses delivered by the implantable Optimzer device proposed for the treatment of chronic heart failure with reduced and midrange ejection fractions (EFs). The Optimizer Smart System (Impulse Dynamics, Orangeburg, New York) is a CCM device that is proposed for the treatment of moderate to severe heart failure. The system comprised of programmable OPTIMIZER Smart Implantable Pulse Generator (IPG), Model CCM X10; port plug, #2 torque wrench for securing the implanted leads

- OMNI Smart Programmer, model OMNI™ II (with OMNI Smart Software)
- OPTIMIZER Smart Charger, model Mini Charger

- Implantable leads: 2 ventricular leads and 1 atrial lead.

CCM® is the brand name for cardiac contractility modulation, the non-excitatory electrical pulses delivered by the implantable Optimzer device. Unlike a pacemaker or a defibrillator, the OPTIMIZER system is designed to control the strength of contraction of the heart muscle rather than the rhythm.

According to the manufacturer's website, the Optimizer system is a device-based treatment option for the approximately seventy percent of CHF patients with advanced symptoms that have normal QRS duration and are not suitable for Cardiac Resynchronization Therapy (CRT). It is a minimally invasive implantable device designed to treat Chronic Heart Failure (CHF) in patients that are symptomatic despite appropriate medical treatment. The device is based on novel Cardiac Contractility Modulation technology and delivers non-excitatory electric pulses. CCM signals are nonexcitatory electrical signals applied during the cardiac absolute refractory period that enhance the strength of cardiac muscular contraction (Abraham, et al., 2018).

U.S. Food and Drug Administration (FDA): The OPTIMIZER Smart System (Impulse Dynamics®) received FDA premarket approval (PMA) March 2019. The device, which delivers Cardiac Contractility Modulation therapy, is indicated to improve 6-minute hall walk distance, quality of life, and functional status of New York Heart Association (NYHA) Class III heart failure patients who remain symptomatic despite guideline directed medical therapy, who are in normal sinus rhythm, are not indicated for Cardiac Resynchronization Therapy, and have a left ventricular ejection fraction ranging from 25% to 45%. On 07/30/2021, the FDA gave approval for commercial distribution of the OPTIMIZER SMART Mini System (P180036/S007).

On October 6, 2021, the FDA approved a modification of labeling for the Optimizer Smart medical device, giving approval for removing the Indications for Use requirement for patients to be in normal sinus rhythm (P180036/S008).

The CCM-D® HF System, which combines Impulse Dynamics®' proprietary CCM® therapy for the treatment of HF symptoms with implantable cardioverter defibrillator (ICD) therapy, is not FDA-approved. The INTEGRA-D™ clinical trial, a multicenter, prospective, single-arm study evaluating the safety and efficacy of CCM-D® HF System in 300 patients, is in progress.

Professional Societies/Organizations: The AHA/ACC/HFSA Guideline for the Management of Heart Failure (Heidenreich, et al., 2022) states:

> 7.4.2. Other Implantable Electrical Interventions
> Cardiac contractility modulation (CCM), a device-based therapy that involves applying relatively high-voltage, long duration electric signals to the RV septal wall during the absolute myocardial refractory period, has been associated with augmentation of LV contractile performance. CCM is FDA-approved for patients with NYHA class III with LVEF of 25% to 45% who are not candidates for CRT. Four RCTs have shown benefits in exercise capacity and QOL but, as of yet, no benefits in death or hospitalizations (Abraham, et al., 2018; Kadish et al., 2011; Borggrefe, et al., 2008; Neelagaru, et al., 2006). Most patients in these trials were class III CHF.

Literature Review: According to Clinicaltrials.gov:

- Arrhythmia Burden in Patients With Impulse Dynamics Optimizer Cardiac Contractility Modulation (CCM) Device Implantation: Retrospective and Prospective Evaluation (NCT05704426) was terminated due to delays.

- Assessment of Implantable CCM in the Heart Failure Group With Higher Ejection Fraction (AIM HIGHer trial, NCT05064709) is recruiting.
- Assessment of the Safety and Efficacy of a Combined Cardiac Contractility Modulation and Implantable Cardioverter Defibrillator Device for Subjects With Heart Failure and Reduced Ejection Fraction (INTEGRA-D trial, NCT05855135). First phase of enrollment of single device for CCM® and ICD therapy was completed June 2025.

Linde et al. (2022) conducted a prospective, multicenter, single-arm pilot study to evaluate the efficacy and safety of CCM (Optimizer device) in heart failure patients with preserved ejection fraction (HFpEF).

- Some of the inclusion criteria included:
  - Baseline ejection fraction ≥50% (echocardiogram, as assessed by the site within 30 days of enrolment and confirmed by the core lab).
  - NYHA class II or III symptoms despite receiving stable optimal medical therapya for at least 30 days based on patient's medical records (chronic stable, not transient or crescendo HF or angina pectoris).
  - Stable optimal medical therapy for HF for 3 months.
- There were 47 individuals who met all the eligibility criteria and were implanted at 17 sites in Europe and Australia and completed the 24-week follow-up study. No patient was lost to follow-up.
- Reported results include a significant improvement in the Kansas City Cardiomyopathy Questionnaire (KCCQ) overall summary score from baseline to 24 weeks (18.0±16.6 points, $p<0.001$) (represents a 37% improvement from baseline). There were three procedure-related complications reported in three patients: two lead dislodgements and one worsening tricuspid regurgitation.
- The authors stated, "The current results are subject to the customary limitations of a pilot study: small sample size, single-arm design with no control group, and hence a potential role of placebo effect for the primary endpoint".

Akhtar et al. (2022) conducted a meta-analysis to review the effect of heart failure therapies on improvement in 6-minute walk distance (6MWD), which was analyzed across randomized controlled trials (RCTs) of drug-based therapy, device-based therapy, autonomic modulation, and exercise in patients with heart failure with reduced ejection fraction (HFrEF).

- The primary outcome was improvement in 6-minute walk distance (6MWD) at follow-up. A total of 4 studies with 847 patients with device-based intervention were identified. Included studies compared cardiac resynchronization therapy (CRT) and cardiac contractility modulation (CCM) with the control. Follow-up duration was six months, and the studies reported change in 6MWD. Overall results showed that device-based therapy (cardiac resynchronization therapy and cardiac contractility modulation), autonomic modulation, and exercise training programs are associated with improvement in 6MWD in patients with HFrEF.

Linde et al. (2022) conducted a prospective, multicenter study to assess the potential benefits of CCM in 47 patients with HF with preserved left ventricular (LV) EF (HFpEF). After CCM device implantation, patients were followed for 24 weeks. The primary efficacy endpoint, mean change in the Kansas City Cardiomyopathy Questionnaire (KCCQ) overall score, improved by 18.0 ± 16.6 points ($p<0.001$). This study is limited by small sample size and lack of comparison.

Fastner et al. (2021) published a retrospective analysis on 174 consecutive patients with chronic heart failure and CCM device implantation between 2002 and 2019, to compare the long-term therapeutic effects of CCM therapy in patients with ischemic (ICM) versus non-ischemic

cardiomyopathy (NICM). Authors used data from the MAnnheim cardIac coNtracTility modulAtIoN obsErvational study (MAINTAINED) study in order to test for such differences in patients with ICM versus NICM. MAINTAINED is a single-center, observational study that retrospectively enrolled all patients with CCM device implantation. Before 2016, 3-lead Optimizer® II, III, or IVs systems were implanted; at later dates, 2-lead Optimizer® Smart devices were implanted.

- Baseline characteristics: 170 (61%) had ICM whereas 67 patients (39%) had NICM. Patients generally had advanced symptoms, with 77% having NYHA class III, 13% having NYHA class IV and 11% having NYHA class II (p = 0.45 between groups).
- There was loss to follow-up: 129 patients were available at 3 years and 84 patients available at 5 years. LVEF improved significantly in both groups (each p < 0.01), while the comparison of changes yielded no statistically significant difference (p = 0.83). There was a mortality rate of 28 (NYHA II group) vs. 35% (NYHA III/IV group) in the overall follow-up period (p = 0.54).
- Reported results include that LVEF was significantly higher in NICM patients after 3 years of CCM therapy (p = 0.0211), and after 5 years, also tricuspid annular plane systolic excursion (TAPSE) of NICM patients was significantly higher (p = 0.0437). There were no differences in other effectiveness parameters.
- Over the entire follow-up period, 35% of all patients died (p = 0.81); only in ICM patients, mortality was lower than predicted at 3 years (35 vs. 43%, p = 0.0395). The authors concluded that NICM patients can expect greater functional improvement in response to CCM therapy than ICM patients. Study limitations include retrospective design, change in number of leads, small sample size, with loss to follow-up.

Yuecel et al. (2025) reported from the MAINTAINED study and the Mannheim Cardiac Resynchronization Therapy Registry (MARACANA), including all patients who received CRTs or CCMs in the authors medical centre in Germany between 2012 and 2021. Yuecel et al. retrospectively compared patients provided with either CRT-Ds (*n* = 220) or CCMs with additional defibrillators (*n* = 105) regarding New York Heart Association classification (NYHA), LVEF, and other benchmarks. Before implantation, CCM patients presented with lower LVEF and worse NYHA (both P<0.05), compared with CRT-D patients. The authors concluded that follow-up improvements in NYHA and LVEF were comparable. HF hospitalizations occurred more often for CCM than CRT-D patients (45.7 vs. 16.8%/patient years, P<0.001). The authors stated that differences in HF hospitalization rates may be due to the more advanced HF of CCM patients at implantation.

Kuschyk et al. (2021) and Fastner et al. (2025) reported on a prospective registry study (CCM-REG) to assess long-term effects of cardiac contractility modulation delivered by the Optimizer Smart system on quality of life, left ventricular ejection fraction (LVEF), mortality and heart failure and cardiovascular hospitalizations. The registry included 503 patients.

- Effects were evaluated in three groupings of LVEF (≤25%, 26–34% and ≥35%) and in patients with atrial fibrillation (AF) and normal sinus rhythm (NSR). Hospitalization rates were compared using a chi-square test. Changes in functional parameters of New York Heart Association (NYHA) class, Minnesota Living with Heart Failure Questionnaire (MLWHFQ) and LVEF were assessed with Wilcoxon signed-rank test, and event-free survival by Kaplan–Meier analysis.
- For the entire cohort and each subgroup, NYHA class and MLWHFQ improved at 6, 12, 18 and 24 months (P < 0.0001). At 24 months, NYHA class, MLWHFQ and LVEF showed an average improvement of 0.6 ± 0.7, 10 ± 21 and 5.6 ± 8.4%, respectively (all P < 0.001). LVEF improved in the entire cohort and in the LVEF ≤25% subgroup with AF and NSR. In the overall cohort, heart failure hospitalizations decreased from 0.74 [95% confidence interval (CI) 0.66–0.82] prior to enrolment to 0.25 (95% CI 0.21–0.28) events per patient-year during 2-year follow-up (P < 0.0001).

- Cardiovascular hospitalizations decreased from 1.04 (95% CI 0.95–1.13) events per patient-year prior to enrolment to 0.39 (95% CI 0.35–0.44) events per patient-year during 2-year follow-up (P < 0.0001). Similar reductions of hospitalization rates were observed in the LVEF, AF and NSR subgroups.
- Estimated survival was significantly better than predicted by the Meta-Analysis Global Group in Chronic Heart Failure (MAGGIC) risk score which predicted mortality at one and three years in the entire cohort and in the LVEF 26–34% and ≥35% subgroups. The study is limited by the lack of randomization and a control group.
- Fastner et al. (2025) reported on a sub-study. The purpose of the study was to evaluate the impact of CCM on HF-related hospitalizations and on LVEF as well as quality of life in heart failure with reduced ejection fraction (HFrEF) patients with QRS duration (QRSd) 120–149 milliseconds (ms) compared to QRSd <120 ms. Among 111 of 455 patients with QRSd 120–149 ms (LVEF 29% ± 9%; 82% NYHA class III), CCM diminished HF-related hospitalization rate by 72% (pre- vs post-implant 0.90 vs 0.25 events per patient-year over 2 years; P<.001). LVEF improved by 7% ± 9% (P = .014 vs baseline), and NYHA class by 0.5 ± 0.7 classes (<0.001 vs baseline). The effect sizes were similar to those in QRSd <120 ms patients. The authors concluded that CCM significantly improved HF control in NYHA III HFrEF patients with moderately prolonged QRSd of 120–149 ms. The improvements in HF-related hospitalizations, LVEF, and NYHA class were similar to those in patients with QRSd <120 ms. The authors noted that their results encourage study of CCM in a large population of intermediate QRS complex (iQRS) patients.

Wiegn et al. (2020) conducted a prospective, multicenter, single-arm study (FIX-HF-5C2 study) to test the performance, safety, and clinical effects of the 2-lead Optimizer Smart System.

- A total of 60 patients were enrolled. Major criteria included:
  - adult subjects with LVEF ≥25% and ≤45% by echocardiography (assessed by core laboratory)
  - NYHA III or ambulatory IV symptoms despite 90 days of guideline-directed heart failure medical therapy (including implantable cardioverter defibrillator when indicated) that was stable for 30 days before enrollment
  - and, not indicated for cardiac resynchronization therapy
- Subjects were evaluated at baseline and again at 12 and 24 weeks after implant. The primary effectiveness end point was an assessment of exercise tolerance measured by peak volume rate of oxygen (VO_2) obtained on cardiopulmonary stress testing (CPX). Changes in peak VO2 from baseline to 24-week follow-up in subjects implanted with the 2-lead system were compared to the changes observed in control group subjects of the prior FIX-HF-5C study (Abraham, et al., 2018).
- A total of 55 subjects (91.7%) completed the 24-week CPX test. In addition, four 24-week CPX tests were deemed inadequate by the core laboratory for which the patients declined requests to repeat testing, resulting in 52 tests for the primary end point analysis. However, to ensure robustness of findings, an additional analysis was performed that included these inadequate tests.
- Report results included that baseline characteristics were similar between FIX-HF-5C and FIX-HF-5C2 subjects except that 15% of FIX-HF-5C2 subjects had permanent atrial fibrillation versus 0% in FIX-HF-5C. CCM delivery did not differ significantly between 2- and 3-lead systems. The change of peak VO2 from baseline to 24 weeks was 1.72 mL/kg per minute greater in the 2-lead device group versus controls. 83.1% of 2-lead subjects compared with 42.7% of controls experienced ≥1 class New York Heart Association improvement (P<0.001). There were decreased Optimizer-related adverse events with the 2-lead system compared with the 3-lead system (0% versus 8%; P=0.03).

- Study limitations include small sample size, loss to follow-up, lack of randomization, and use of a historical control group.

Giallauria et al. (2020) performed an individual patient data meta-analysis of prospective trials of CCM that have measured functional capacity and/or quality of life questionnaires in patients with HF. Primary outcomes of interest were peak oxygen consumption (peak VO2), 6 min walk test distance, and quality of life (from established survey).

- Five trials were identified, four randomized studies enrolling 801 participants for all endpoints of interest, and for peak VO_2 alone (n = 60), there was an additional single arm non-randomized trial (FIX-HF-5C2) with a prospective comparison of its 24 week peak VO_2 data compared with the control group of the FIX-HF-5C control patients.
- Pooled analysis showed that, compared with control, CCM significantly improved peak VO_2 ($P < 0.00001$), 6 min walk test distance ($P = 0.005$), and quality of life measured by MLWHFQ ($P < 0.00001$). The authors noted study limitations include that the studies analyzed differed in study design limiting our ability to define representative results across different patient subgroups. They also noted that study cohorts are relatively young and predominantly male; therefore, future data would be needed in older individuals and in more women.

Mando et al. (2019) performed a meta-analysis of the randomized clinical trials (RCTs) to assess the efficacy and safety of CCM therapy. Outcomes of interest were peak oxygen consumption (peak VO2), 6-Minute Walk Distance (6MWD), Minnesota Living with Heart Failure Questionnaire (MLHFQ), HF hospitalizations, cardiac arrhythmias, pacemaker/ICD malfunctioning, all-cause hospitalizations, and mortality. Data were expressed as standardized mean difference (SMD) or odds ratio (OR).

- Four RCTs including 801 patients (CCM n = 394) were available for analysis. The mean age was 59.63 ± 0.84 years, mean ejection fraction was 29.14 ± 1.22%, and mean QRS duration was 106.23 ± 1.65 msec. Mean follow-up duration was six months.
- CCM was associated with improved MLWHFQ ($p = 0.0008$). There were no differences in HF hospitalizations ($p = 0.12$), 6MWD ($p = 0.10$), arrhythmias ($p = 0.14$), pacemaker/ICD malfunction/sensing defect ($p = 0.06$), all-cause hospitalizations ($p = 0.33$), or all-cause mortality ($p = 0.92$) between the CCM and non-CCM groups.
- The authors concluded that short-term treatment with CCM may improve MLFHQ without significant difference in 6MWD, arrhythmic events, HF hospitalizations, all-cause hospitalizations, and all-cause mortality and that there is a trend towards increased pacemaker/ICD device malfunction. They noted that larger RCTs may be needed to determine if the CCM therapy will be beneficial with longer follow-up.

Anker et al. (2019) conducted prospective registry study with the aim to assess the longer-term impact of cardiac contractility modulation (CCM) on hospitalizations and mortality in real-world experience.

- The study included 140 patients with 25% ≤ left ventricular ejection fraction (LVEF) ≤ 45% receiving CCM therapy (CCM-REG25-45) for clinical indications. Cardiovascular and heart failure (HF) hospitalizations, Minnesota Living with Heart Failure Questionnaire (MLHFQ) and NYHA class were assessed over 2 years. Mortality was tracked through 3 years and compared with predictions by the Seattle Heart Failure Model (SHFM). Separate analysis was performed on patients with 35% ≤ LVEF ≤ 45% (CCM-REG35-45) and 25% ≤ LVEF < 35% (CCM-REG25-34).
- Hospitalizations decreased by 75% (from 1.2/patient-year the year before, to 0.35/patient-year during the 2 years following CCM, $P<0.0001$) in CCM-REG25-45 and by a similar

amount in CCM-REG35-45 (P<0.0001) and CCM-REG25-34. MLHFQ and NYHA class improved in all three cohorts, with progressive improvements over time (P<0.002).
- Three-year survival in CCM-REG25-45 (82.8%) and CCM-REG24-34 (79.4%) were similar to those predicted by SHFM (76.7%, P = 0.16; 78.0%, P = 0.81, respectively) and was better than predicted in CCM-REG35-45 (88.0% vs. 74.7%, P = 0.046). The limitations of the study include lack of randomization and no separate control group.

Abraham et al. (2018) conducted a randomized controlled study (the FIX-HF-5C study) to confirm a subgroup analysis of the prior FIX-HF-5 (Evaluate Safety and Efficacy of the OPTIMIZER System in Subjects With Moderate-to-Severe Heart Failure) study to evaluate that cardiac contractility modulation (CCM) improved exercise tolerance (ET) and quality of life in patients with ejection fractions between 25% and 45%.
- The study included 160 patients with NYHA functional class III or IV symptoms, QRS duration <130 ms, and ejection fraction ≥25% and ≤45% that were randomized to continued medical therapy (control, n=86) or CCM (treatment, n=74; 68 underwent device implantation) unblinded for 24 weeks. Peak rate of oxygen consumption (peak Vo_2) (primary endpoint), Minnesota Living With Heart Failure questionnaire, NYHA functional class, and 6-min hall walk were measured at baseline and at 12 and 24 weeks.
- The difference in peak Vo_2 between groups was 0.84 ml O_2/kg/min. Minnesota Living With Heart Failure questionnaire (p < 0.001), NYHA functional class (p < 0.001), and 6-min hall walk (p = 0.02) were all better in the treatment versus control group. There were seven device-related events, yielding a lower bound of 80% of patients free of events. The composite of cardiovascular death and HF hospitalizations was reduced from 10.8% to 2.9% (p = 0.048). Limitation of the study include limited follow-up duration of the current study which limits the ability to evaluate the long-term effects of CCM on mortality and hospitalizations.

Müller et al. (2017) reported on a prospective, two-year, multi-site evaluation of CCM in patients with heart failure.
- The study included 143 subjects with heart failure and reduced ejection fraction that were followed via clinical registry for 24 months recording NYHA class, Minnesota living with heart failure questionnaire (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%).
- One hundred and six subjects from 24 sites completed the 24-month follow-up. Baseline parameters were similar among LVEF groups. NYHA and MLWHFQ improved in all three 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.
- There were 18 deaths (seven cardiovascular related) over two years. Overall survival at two years was 86.4% (95% confidence intervals: 79.3, 91.2%). The study is limited by the lack of randomization and control group.

Röger et al. (2017) conducted a prospective blinded randomized trial including 48 patients to compare the efficacy and safety of CCM when the signal is delivered through one vs. two ventricular leads.
- Patients had symptomatic heart failure (NYHA Classes II–III) and reduced left ventricular ejection fraction. All patients received a CCM system with two ventricular leads and were

randomized to CCM active through both or just one ventricular lead; 25 patients were randomized to receive signal delivery through two leads (Group A) and 23 patients to signal delivery through one lead (Group B). The study compared the mean changes from baseline to 6 months follow-up in peakVO_2, NYHA classification, and quality of life (by MLWHFQ).
- The efficacy and safety of CCM in this study were similar when the signal was delivered through either one or two ventricular leads. The authors noted their results support the potential use of a single ventricular lead for delivery of CCM.

Kadish et al. (2011) conducted a randomized controlled trial (FIX-HF-5 trial) to test the longer-term safety and efficacy of CCM treatment.
- The study tested CCM in 428 New York Heart Association class III or IV, narrow QRS heart failure patients with ejection fraction (EF) ≤ 35% randomized to optimal medical therapy (OMT) plus CCM (n = 215) versus OMT alone (n = 213). Efficacy was assessed by ventilatory anaerobic threshold (VAT), primary end point, peak Vo_2 (pVo_2), and Minnesota Living with Heart Failure Questionnaire (MLWFQ) at six 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 (12.5% allowable delta). The groups were comparable for age, EF, pVo_2 and other characteristics.
- While VAT did not improve at six months, CCM significantly improved pVo_2 and MLWHFQ [P = .024] and [P < .0001], respectively) over OMT. Forty-eight percent of OMT and 52% of CCM patients experienced a safety end point, which satisfied non-inferiority criterion (P = .03). Post hoc, hypothesis-generating analysis identified a subgroup (characterized by baseline EF ≥ 25% and New York Heart Association class III symptoms) in which all parameters were improved by CCM.
- The authors noted that based on the prespecified primary end point, CCM efficacy was not demonstrated, and further studies will be required to determine the role of CCM in the treatment of patients with medically refractory heart failure.

INFERIOR VENA CAVA SENSOR

An inferior vena cava (IVC) sensor was developed on the hypothesis that changes in IVC area and collapsibility (from increasing volume) occur earlier than changes in markers currently used to predict impending decompensation and would thereby facilitate prompt intervention to manage fluid status and prevent decompensation. NORM has three components: The first is a sensor that is placed in the IVC vein. The second is a belt worn for a few minutes a day. The third is an app on the patient's phone, and a corresponding app/portal on the system of the patient's provider.

U.S. Food and Drug Administration (FDA): According to the Diagnostic and Interventional Cardiology website, the Fire1 System Received FDA Breakthrough Device Designation in January 2025. According to the Cardiovascular Business website, the IVC-based heart failure management technology, now being marketed under the brand name Norm, was developed by in a medical device incubator in California by FIRE1 (Foundry Innovation and Research 1), an Irish medtech company. The goal is to measure changes in a patient's IVC area and collapsibility, which can help anticipate when heart failure events might occur earlier than other available heart failure monitors. The Norm system includes an implantable sensor, a pusher and loader for delivering that sensor to the IVC, an external hardware unit with a belt and a web application.

Professional Societies/Organizations: The AHA/ACC/HFSA Guideline for the Management of Heart Failure (Heidenreich, et al., 2022) does not address an implantable inferior vena cava (IVC) sensor.

Literature Review: Kalra et al. (2025) reported initial (3 month) results of the first-in-human study (FUTURE-HF [First in Human Clinical Investigation of the FIRE1 System in Heart Failure Patients], NCT04203576) of the IVC management system (FIRE1). FUTURE-HF is a prospective, multicenter, nonrandomized, single-arm study to evaluate the safety and feasibility of an implantable sensor and external monitoring system to remotely measure and manage IVC area and collapsibility. Kalra et al. reported on the fully enrolled study, with analysis conducted on data collected up to December 10, 2024.

- Patients with HF hospitalizations within the previous year, with elevated natriuretic peptide levels, and on optimal HF treatment were included. Patients had to have experienced HF decompensation events (defined as either hospitalization for HF or HF treatment in a hospital day care setting or urgent outpatient HF visit) within the previous 12 months and/or were required to have certain brain natriuretic peptide (BNP) findings.
- The primary safety endpoints were procedural success without device- or procedure-related complications at 3 months. The primary technical endpoint was signal acquisition following implantation and at a clinic visit within 3 months.
- Sensor-derived IVC area was compared with computed tomography (CT)– based IVC dimensions.

Results demonstrated:

- 50 underwent successful implantation with 49 contributing to the primary safety and technical endpoints at 3 months.
- Sensor-derived IVC area demonstrated excellent agreement with CT measurement (mean absolute error 13.53 mm^2 [3.55%] R^2 = 0.98).
- There were no thrombotic or other device or procedure-related serious adverse events (AEs) recorded.

The authors concluded that the implantation of a novel IVC sensor was "safe and feasible in patients with HF. The sensor-derived IVC area demonstrated excellent correlation with CT-derived IVC dimensions and may serve as a novel ambulatory congestion management tool for remote care in HF".

The FUTURE-HF2 Trial [First in Human Clinical Investigation of the FIRE1 System in Heart Failure Patients] is a prospective, multicenter, single-arm, early feasibility study of 15 patients with HF (irrespective of ejection fraction) and with an HF event in the previous 12 months, an elevated NT-proBNP level, and receiving ≥ 40 mg of furosemide equivalent. Primary endpoints included successful deployment without procedure-related (30 days) or sensor-related complications (3 months) and successful data transmission to a secure database (3 months). All 15 patients reached the primary safety endpoint at 30 days and both the primary safety and effectiveness end points at 3 months (Uriel, et al., 2025; NCT05763407).

Health Equity Considerations

Health equity is the highest level of health for all people; health inequity is the avoidable difference in health status or distribution of health resources due to the social conditions in which people are born, grow, live, work, and age.

Social determinants of health are the conditions in the environment that affect a wide range of health, functioning, and quality of life outcomes and risks. Examples include safe housing, transportation, and neighborhoods; racism, discrimination and violence; education, job

opportunities and income; access to nutritious foods and physical activity opportunities; access to clean air and water; and language and literacy skills.

Blacks have a higher incidence of HF and disproportionately have poor outcomes related to HF compared with whites. These racial differences in HF outcomes are caused, in part, by the higher prevalence of clinical risk factors for HF such as uncontrolled hypertension, endothelial dysfunction, and deleterious genetic polymorphisms among nonwhites. Before 50 years of age, HF is more common among Blacks than whites. This higher risk is considered to be the result of differences in the prevalence of hypertension, diabetes mellitus, and low socioeconomic status (SES). Women with HF report worse health-related quality of life than men with HF. Women differ from men in clinical symptoms and experience more morbidity, particularly decreased functional status and depression. Generally speaking, the treatment guidelines for men and women are the same, although women have been underrepresented in trials evaluating HF therapy (White-Williams, et al., 2020).

Medicare Coverage Determinations

	Contractor	Determination Name/Number	Revision Effective Date
NCD	National	No Determination found.	
LCD		No Determination found	

Note: Please review the current Medicare Policy for the most up-to-date information.
(NCD = National Coverage Determination; LCD = Local Coverage Determination)

Appendix

*Applying ACC/AHA Class of Recommendation and Level of Evidence to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care

The Class (Strength) of Recommendation (COR) indicates the strength of recommendation, encompassing the estimated magnitude and certainty of benefit in proportion to risk.

Class I – Strong (is recommended)
Class 2a – Moderate (is reasonable)
Class 2b – Weak (may/might be reasonable)
Class 3 – No benefit (Moderate) (is not recommended)
Class 3 – Harm (Strong) (potentially harmful)

The Level (Quality) of Evidence (LOE) rates the quality of scientific evidence supporting the intervention on the basis of the type, quantity, and consistency of data from clinical trials and other sources.

Level A – High quality evidence from more than one randomized clinical trial, Meta-analyses of high-quality randomized clinical trials, One or more randomized clinical trials corroborated by high-quality registry.
Level B-R – Randomized. Moderate quality evidence from one or more randomized clinical trials, Meta-analyses of moderate-quality randomized clinical trials.
Level B-NR – Non-randomized. Moderate quality evidence from one or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies, Meta-analyses of such studies.

Level C-LD – Limited data. Randomized or nonrandomized observational or registry studies with limitations of design or execution, Meta-analyses of such studies, Physiological or mechanistic studies of human subjects.
Level C-EO – Expert Opinion. Consensus expert opinion based on the clinical experience

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Revision Details

Type of Revision	Summary of Changes	Date
Annual Review	• Added codes to an existing policy statement	01/15/2026
Focused Review	• Added new policy statement for inferior vena cava sensor • Revised policy statement for carotid sinus baroreflex activation device	8/15/2025

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Focused Review	• Added new policy statement for left atrial pressure sensor • Revised policy statement for carotid sinus baroreflex activation device • Revised policy statement for pulmonary artery pressure sensor • Revised policy statement for cardiac contractility modulation therapy	3/15/2025
Focused Review	• Removed policy statement and content related to coronary intravascular lithotripsy	12/30/2024
Focused review	• Revised policy statement for carotid sinus baroreflex activation device • Revised policy statement for cardiac contractility modulation therapy	12/15/2024
Focused review	• Removed content for: Endovascular repair of iliac artery at the time of aorto-iliac artery endograft placement by deployment of an iliac branched endograft (i.e., GORE® EXCLUDER® Iliac Branch Endoprosthesis [IBE] device	11/01/2024
New Coverage Policy topic and Annual Review of four cardiac topics previously located in CP 0504 Omnibus Codes.	• Added new policy statement for carotid sinus baroreflex activation device (i.e., BAROSTIM™ NEO® System) (New topic) • No clinical policy statement changes from CP 0504 Omnibus Codes: ➢ Endovascular repair of iliac artery at the time of aorto-iliac artery endograft placement by deployment of an iliac branched endograft (i.e., GORE® EXCLUDER® Iliac Branch Endoprosthesis [IBE] device ➢ Pulmonary artery pressure sensor (e.g., CardioMEMS™ HF system, Cordella™ Pulmonary Artery Sensor System) ➢ Cardiac contractility modulation (CCM®) therapy (i.e., OPTIMIZER Smart System) ➢ Coronary Intravascular Lithotripsy (IVL) (i.e., Shockwave C2 Coronary IVL System)	10/15/2024

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