

Protocol

Biventricular Pacemakers (Cardiac Resynchronization Therapy) for the Treatment of Heart Failure

(20210)

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|-------------------------|----|---------------------------------------------------------------------------------------------------------|--------------------------------|
| Medical Benefit | | Effective Date: 07/01/15 | Next Review Date: 05/19 |
| Preauthorization | No | Review Dates: 09/09, 01/10, 09/10, 07/11, 07/12, 09/12, 05/13, 05/14, 05/15, 05/16, 05/17, 05/18 | |

Preauthorization is not required.

The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.

| Populations | Interventions | Comparators | Outcomes |
|------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Individuals: <ul style="list-style-type: none"> With New York Heart Association class III or IV heart failure | Interventions of interest are: <ul style="list-style-type: none"> Cardiac resynchronization therapy with or without defibrillator | Comparators of interest are: <ul style="list-style-type: none"> Medical care Medical care plus defibrillator | Relevant outcomes include: <ul style="list-style-type: none"> Overall survival Symptoms Functional outcomes Quality of life Hospitalizations Treatment-related morbidity |
| Individuals: <ul style="list-style-type: none"> With New York Heart Association class II heart failure | Interventions of interest are: <ul style="list-style-type: none"> Cardiac resynchronization therapy with or without defibrillator | Comparators of interest are: <ul style="list-style-type: none"> Medical care Medical care plus defibrillator | Relevant outcomes include: <ul style="list-style-type: none"> Overall survival Symptoms Functional outcomes Quality of life Hospitalizations Treatment-related morbidity |
| Individuals: <ul style="list-style-type: none"> With New York Heart Association class I heart failure | Interventions of interest are: <ul style="list-style-type: none"> Cardiac resynchronization therapy with or without defibrillator | Comparators of interest are: <ul style="list-style-type: none"> Medical care Medical care plus defibrillator | Relevant outcomes include: <ul style="list-style-type: none"> Overall survival Symptoms Functional outcomes Quality of life Hospitalizations Treatment-related morbidity |
| Individuals: <ul style="list-style-type: none"> With heart failure and atrial fibrillation | Interventions of interest are: <ul style="list-style-type: none"> Cardiac resynchronization therapy with or without defibrillator | Comparators of interest are: <ul style="list-style-type: none"> Medical care Medical care plus defibrillator | Relevant outcomes include: <ul style="list-style-type: none"> Overall survival Symptoms Functional outcomes Quality of life Hospitalizations Treatment-related morbidity |

| Populations | Interventions | Comparators | Outcomes |
|--------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Individuals: <ul style="list-style-type: none"> With heart failure and atrioventricular nodal block | Interventions of interest are: <ul style="list-style-type: none"> Cardiac resynchronization therapy | Comparators of interest are: <ul style="list-style-type: none"> Medical care Medical care plus defibrillator | Relevant outcomes include: <ul style="list-style-type: none"> Overall survival Symptoms Functional outcomes Quality of life Hospitalizations Treatment-related morbidity |
| Individuals: <ul style="list-style-type: none"> With heart failure | Interventions of interest are: <ul style="list-style-type: none"> Triple-site cardiac resynchronization therapy | Comparators of interest are: <ul style="list-style-type: none"> Standard cardiac resynchronization therapy | Relevant outcomes include: <ul style="list-style-type: none"> Overall survival Symptoms Functional outcomes Quality of life Hospitalizations Treatment-related morbidity |
| Individuals: <ul style="list-style-type: none"> With heart failure | Interventions of interest are: <ul style="list-style-type: none"> Cardiac resynchronization therapy combined with remote fluid monitoring | Comparators of interest are: <ul style="list-style-type: none"> Standard cardiac resynchronization therapy only | Relevant outcomes include: <ul style="list-style-type: none"> Overall survival Symptoms Functional outcomes Quality of life Hospitalizations Treatment-related morbidity |

DESCRIPTION

Cardiac resynchronization therapy (CRT), which consists of synchronized pacing of the left and right ventricles, is intended to treat patients with heart failure and dyssynchronous ventricular contractions. Treatment involves placement of a device that paces both ventricles and coordinates ventricular pacing to maximize cardiac pumping function and left ventricular ejection fraction (LVEF).

SUMMARY OF EVIDENCE

For individuals who have New York Heart Association (NYHA) class III or IV heart failure with a left ventricular ejection fraction (LVEF) of 35% or less who are in sinus rhythm, treated with guideline-directed medical therapy, and have either left bundle branch block (LBBB) or a QRS interval of 150 ms or more who receive CRT with or without defibrillator, the evidence includes randomized controlled trials (RCTs) and systematic reviews of RCTs. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, hospitalizations, and treatment-related morbidity. There is a large body of clinical trial evidence supporting use of CRT in patients with NYHA class III or IV heart failure. The RCTs have consistently reported that CRT treatment reduces mortality, improves functional status, and improves quality of life for patients with NYHA class III or IV heart failure. Multiple subgroup analyses of RCTs have demonstrated that the benefit of CRT is mainly restricted to patients with LBBB or QRS interval greater than 150 ms. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have NYHA class II heart failure with a LVEF of 30% or less who are in sinus rhythm, treated with guideline-directed medical therapy, and have either LBBB or a QRS interval of 150 ms or more who receive CRT with or without defibrillator, the evidence includes RCTs and systematic reviews of RCTs. Relevant outcomes

are overall survival, symptoms, functional outcomes, quality of life, hospitalizations, and treatment-related morbidity. For patients with NYHA class II heart failure, at least four RCTs assessing CRT have been published. A mortality benefit was reported in one of the four trials, the RAFT trial. None of the other three RCTs reported a mortality difference, but a subgroup analysis of the MADIT-CRT trial reported a mortality benefit for patients with LBBB. Among other outcome measures, hospitalizations for heart failure showed consistent improvements, but quality of life and functional status did not. Multiple subgroup analyses of RCTs have demonstrated that the benefit of CRT is mainly restricted to patients with LBBB or a QRS interval greater than 150 ms. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have NYHA class I heart failure who receive CRT with or without defibrillator, the evidence includes RCTs and systematic reviews of RCTs. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, hospitalizations, and treatment-related morbidity. Few patients with NYHA class I heart failure have been included in RCTs. The MADIT-CRT trial included 265 patients with class I. While the treatment effect on death and hospitalization favored combined implantable cardiac defibrillator (ICD) plus CRT devices versus ICD alone for class I patients, the confidence interval was large and included a 25% to 30% increase in events. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have heart failure and atrial fibrillation who receive CRT with or without defibrillator, the evidence includes four RCTs and observational studies. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, hospitalizations, and treatment-related morbidity. Data from RCTs have reported conflicting results, with one reporting improvements for patients with atrial fibrillation and others reporting no significant improvements. Results from observational studies are also conflicting. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have heart failure and atrioventricular (AV) nodal block who receive CRT, the evidence includes RCTs and systematic reviews of RCTs. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, hospitalizations, and treatment-related morbidity. One large RCT demonstrated that CRT led to improvements in heart failure-related hospitalizations and urgent care visits among patients with heart failure and AV block but who would not necessarily meet conventional criteria for CRT. For patients who require ventricular pacing but have no left ventricular dysfunction, results of one small RCT have suggested that biventricular pacing is associated with improved measures of cardiac function, but the trial was small and underpowered to detect differences in clinical outcomes. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have heart failure who receive triple-site CRT, the evidence includes small RCTs. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, hospitalizations, and treatment-related morbidity. The available RCTs have reported improved outcomes on at least one measure of functional status or quality of life with triple-site CRT compared to conventional CRT. However, the trials are small and have methodologic limitations. In addition, outcomes reported differed across studies. Triple-site CRT was also associated with higher radiation exposure and a greater number of additional procedures postimplantation. Larger, high-quality RCTs are needed to better define the benefit-risk ratio for triple-site CRT compared to conventional CRT. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have heart failure who receive CRT combined with remote fluid monitoring, the evidence includes three RCTs. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, hospitalizations, and treatment-related morbidity. Three RCTs have reported no improvement in outcomes associated with remote fluid monitoring for patients with heart failure. The evidence is insufficient to determine the effects of the technology on health outcomes.

POLICY

Biventricular pacemakers with or without an accompanying implantable cardiac defibrillator (i.e., a combined biventricular pacemaker plus implantable cardiac defibrillator) may be considered **medically necessary** as a treatment of heart failure in patients who meet all of the following criteria:

NEW YORK HEART ASSOCIATION CLASS III OR IV

- Left ventricular ejection fraction $\leq 35\%$
- Sinus rhythm
- Patients treated with guideline-directed medical therapy (see Policy Guidelines)

AND

- Either left bundle branch block OR QRS interval ≥ 150 ms

NEW YORK HEART ASSOCIATION CLASS II

- Left ventricular ejection fraction $\leq 30\%$
- Sinus rhythm
- Patients treated with a guideline-directed medical therapy (see Policy Guidelines)

AND

- Either Left bundle branch block, OR QRS duration ≥ 150 ms

For patients who do not meet the criteria outlined above, but have an indication for a ventricular pacemaker or biventricular pacemakers with or without an accompanying implantable cardiac defibrillator (i.e., a combined biventricular pacemaker/implantable cardiac defibrillator) may be considered **medically necessary** as an alternative to a right ventricular pacemaker in patients who meet all of the following criteria:

- New York Heart Association (NYHA) class I, II, III, or IV heart failure;
- Left ventricular ejection fraction $\leq 50\%$;
- The presence of atrioventricular block with requirement for a high percentage of ventricular pacing (see Policy Guidelines); and
- Patients treated with guideline-directed medical therapy (see Policy Guidelines).

Biventricular pacemakers, with or without an accompanying implantable cardiac defibrillator (i.e., a combined biventricular pacemaker plus implantable cardiac defibrillator), are considered **investigational** as a treatment for patients with NYHA class I heart failure who do not meet the above criteria.

Biventricular pacemakers, with or without an accompanying implantable cardiac defibrillator (i.e., a combined biventricular pacemaker plus implantable cardiac defibrillator), are considered **investigational** as a treatment for heart failure in patients with atrial fibrillation who do not meet the above criteria.

Triple-site (triventricular) cardiac resynchronization therapy, using an additional pacing lead, is considered **investigational**.

An intrathoracic fluid monitoring sensor is considered **investigational** as a component of a biventricular pacemaker.

POLICY GUIDELINES

DEFINITIONS

AV block with a requirement for a high percentage of ventricular pacing is considered to be present when there is either:

- Third-degree AV block; or
- Second-degree AV block or a PR interval of 300 ms or more when paced at 100 beats per minute.

Guideline-directed medical therapy for heart failure is outlined in 2013 American College of Cardiology Foundation and American Heart Association guidelines for the management of heart failure (Yancy et al, 2013).

BACKGROUND

It is estimated that 20% to 30% of patients with heart failure have intraventricular conduction disorders resulting in a contraction pattern that is not coordinated and a wide QRS interval on the electrocardiogram. This abnormality appears to be associated with increased morbidity and mortality. Biventricular pacemakers using three leads (one in the right atrium, one in each ventricle), also known as CRT, have been investigated as a technique to coordinate the contraction of the ventricles, thus improving patients' hemodynamic status. Several types of CRT devices are available, including those that incorporate biventricular pacing into automatic ICDs, stand-alone biventricular pacemakers, and biventricular pacemakers that incorporate fluid monitoring via bioimpedance.

Originally developed CRT devices typically used two ventricular leads for biventricular pacing. Devices and implantation techniques have been developed to allow for multisite pacing, with the goal of improving CRT response. This may be accomplished in one of two ways: through the use of multiple leads within the coronary sinus (triventricular pacing) or through the use of multipolar left ventricular pacing leads, which can deliver pacing stimuli at multiple sites.

REGULATORY STATUS

There are numerous CRT devices, combined ICD plus CRT devices (CRT-D), and combined CRT plus fluid monitoring devices. Some devices are discussed here. For example, in 2001, the InSync® Biventricular Pacing System (Medtronic), a stand-alone biventricular pacemaker, was approved by the U.S. Food and Drug Administration (FDA) through the premarket approval process for the treatment of patients with NYHA class III or IV heart failure, on a stable pharmacologic regimen, who also have a QRS duration of 130 ms or longer and a LVEF of 35% or less. Devices by Guidant (CONTAK CD® CRT-D System) and Medtronic (InSync® ICD Model 7272) have been approved by the FDA through the premarket approval process for combined cardiac resynchronization therapy defibrillators for patients at high risk of sudden cardiac death due to ventricular arrhythmias and who have NYHA class III or IV heart failure with a LVEF of 35% or less, QRS interval 130 ms or longer (≥ 120 ms for the Guidant device), and remain symptomatic despite a stable, optimal heart failure drug therapy. In 2006, Biotronik Inc. received premarket approval from FDA for its combined ICD-D device with ventricular pacing leads (Tupos LV/ATx CRT-D/Kronos LV-T CRT-D systems¹); in 2013, the company received FDA approval for updated ICD-D devices (Ilesto/Iforia series).²

In September 2010, FDA expanded indications for some CRT devices to include patients with class I and II heart failure. Based on data from the MADIT-CRT study, indications for three Guidant (Boston Scientific) CRT-D (Cognis®, Livian®, and Contak Renewal) devices were expanded to include patients with heart failure who

receive stable optimal pharmacologic therapy for heart failure and who meet any of the following classifications³:

- Moderate-to-severe heart failure (NYHA class III-IV) with an ejection fraction less than 35% and QRS interval greater than 120 ms.
- Left bundle branch block with a QRS interval greater than or equal to 130 ms, ejection fraction less than 30%, and mild (NYHA class II) ischemic or nonischemic heart failure or asymptomatic (NYHA class I) ischemic heart failure.

In April 2014, the FDA further expanded indications for multiple Medtronic CRT devices to include patients with NYHA class I, II, or III heart failure, who have a LVEF of 50% or less on stable, optimal heart failure medical therapy, if indicated, and have AV block that is expected to require a high percentage of ventricular pacing that cannot be managed with algorithms to minimize right ventricular pacing. The expanded indication was based on data from the BLOCK-HF study, a Medtronic-sponsored randomized controlled trial that evaluated use of CRT in patients with NYHA class I, II, or III heart failure, LVEF of 50% or less, and AV block.

Several CRT devices have incorporated a fourth lead, providing quadripolar pacing. The Medtronic Viva™ Quad XT and the Viva Quad S have a fourth lead, and the Medtronic Attain Performa® has a left ventricular lead, which received clearance for marketing from FDA in August 2014. The Dynagen™ X4 and Inogen™ X4 devices (Boston Scientific, Marlborough, MA) also incorporate a fourth lead. Other CRT devices with quadripolar leads have been approved for use outside of the United States (e.g., St. Jude Quartet™ left ventricular lead).

Multiple devices manufactured by Medtronic combine a CRT with the OptiVol™ monitoring system. For example, in 2005, the InSync Sentry® system was approved by FDA through the supplemental premarket approval process. This combined biventricular pacemaker plus ICD is also equipped to monitor intrathoracic fluid levels using bioimpedance technology, referred to as OptiVol™ Fluid Status Monitoring. Bioimpedance measures, defined as the electrical resistance of tissue to flow of current, are performed many times a day using a vector from the right ventricular coil on the lead in the right side of the heart to the implanted pacemaker devices; changes in bioimpedance reflect intrathoracic fluid status and are evaluated using a computer algorithm. For example, changes in a patient's daily average of intrathoracic bioimpedance can be monitored; differences in the daily average are compared with a baseline and reported as the OptiVol™ Fluid Index. It has been proposed that these data may be used as an early warning system of cardiac decompensation or may provide feedback that enables a physician to tailor medical therapy.

FDA product code: NIK

RELATED PROTOCOL

Implantable Cardioverter Defibrillators

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

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We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

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