Protocol

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

(20210)

Medical Benefit		**Effective Date**: 08/01/20	**Next Review Date**: 05/21
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, 05/19, 05/20	

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: • With New York Heart Association class III or IV heart failure with left ventricular ejection fraction <35%	Interventions of interest are: • Cardiac resynchronization therapy with or without defibrillator	Comparators of interest are: • Medical care • Medical care plus defibrillator	Relevant outcomes include: • Overall survival • Symptoms • Functional outcomes • Quality of life • Hospitalizations • Treatment-related morbidity
Individuals: • With New York Heart Association class II heart failure with left ventricular ejection fraction <30%	Interventions of interest are: • Cardiac resynchronization therapy with or without defibrillator	Comparators of interest are: • Medical care • Medical care plus defibrillator	Relevant outcomes include: • Overall survival • Symptoms • Functional outcomes • Quality of life • Hospitalizations • Treatment-related morbidity
Individuals: • With New York Heart Association class I heart failure	Interventions of interest are: • Cardiac resynchronization therapy with or without defibrillator	Comparators of interest are: • Medical care • Medical care plus defibrillator	Relevant outcomes include: • Overall survival • Symptoms • Functional outcomes • Quality of life • Hospitalizations • Treatment-related morbidity
Individuals: • With New York Heart Association class I, II, III or IV heart failure with left ventricular ejection fraction <50% and atrioventricular block	Interventions of interest are: • Cardiac resynchronization therapy with or without defibrillator	Comparators of interest are: • Medical care • Medical care plus defibrillator	Relevant outcomes include: • Overall survival • Symptoms • Functional outcomes • Quality of life • Hospitalizations • Treatment-related morbidity

Populations	Interventions	Comparators	Outcomes
Individuals: • With heart failure and atrial fibrillation	Interventions of interest are: • Cardiac resynchronization therapy with or without defibrillator	Comparators of interest are: • Medical care • Medical care plus defibrillator	Relevant outcomes include: • Overall survival • Symptoms • Functional outcomes • Quality of life • Hospitalizations • Treatment-related morbidity
Individuals: • With heart failure and atrioventricular nodal block	Interventions of interest are: • Cardiac resynchronization therapy	Comparators of interest are: • Medical care	Relevant outcomes include: • Overall survival • Symptoms • Functional outcomes • Quality of life • Hospitalizations • Treatment-related morbidity
Individuals: • With heart failure	Interventions of interest are: • Triple-site cardiac resynchronization therapy	Comparators of interest are: • Standard cardiac resynchronization therapy	Relevant outcomes include: • Overall survival • Symptoms • Functional outcomes • Quality of life • Hospitalizations • Treatment-related morbidity
Individuals: • With heart failure	Interventions of interest are: • Cardiac resynchronization therapy combined with remote fluid monitoring	Comparators of interest are: • Standard cardiac resynchronization therapy only	Relevant outcomes include: • 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.

SUMMARY OF EVIDENCE

For individuals who have New York Heart Association (NYHA) class III or IV heart failure with a left ventricular ejection fraction 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. The relevant outcomes are overall survival (OS), symptoms, functional outcomes, quality of life (QOL), hospitalizations, and treatment-related morbidity. There is a large body of clinical trial evidence supporting the use of CRT in patients with NYHA class III or IV heart failure. The RCTs have consistently reported that CRT reduces mortality, improves functional status, and improves QOL 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 left ventricular ejection fraction 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. The relevant outcomes are OS, symptoms, functional outcomes, QOL, 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 Resynchronization-Defibrillation for Ambulatory Heart Failure Trial. None of the other three RCTs reported a mortality difference, but a subgroup analysis of the Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy trial reported a mortality benefit for patients with LBBB. Among other outcome measures, hospitalizations for heart failure showed consistent reductions, but QOL and functional status did not improve. 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. The relevant outcomes are OS, symptoms, functional outcomes, QOL, hospitalizations, and treatment-related morbidity. Few patients with NYHA class I heart failure have been included in RCTs. The Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy trial included 265 patients with class I. While the treatment effect on death and hospitalization favored combined implantable cardiac defibrillator plus CRT devices vs. implantable cardiac defibrillator 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 NYHA class I, II, III or IV heart failure with left ventricular ejection fraction of 50% or less and the presence of atrioventricular block with requirement for a high percentage of ventricular pacing, treated with guideline-directed medical therapy, who receive CRT with or without defibrillator, the evidence includes RCTs and systematic reviews of RCTs. The relevant outcomes are OS, symptoms, functional outcomes, QOL, hospitalizations, and treatment-related morbidity. For patients who have atrioventricular nodal block, some degree of left ventricular dysfunction, and who would not necessarily meet conventional criteria for CRT but would require ventricular pacing, a large RCT has demonstrated improvements in heart failure-related hospitalizations and urgent care visits among patients treated with CRT instead of RV pacing alone. For patients who require ventricular pacing but have no left ventricular dysfunction, results of a 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 and atrial fibrillation who receive CRT with or without defibrillator, the evidence includes four RCTs and observational studies. The relevant outcomes are OS, symptoms, functional outcomes, QOL, hospitalizations, and treatment-related morbidity. Results from RCTs have been conflicting, 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 nodal block who receive CRT, the evidence includes RCTs and systematic reviews of RCTs. The relevant outcomes are OS, symptoms, functional outcomes, QOL, hospitalizations, and treatment-related morbidity. One large RCT demonstrated that CRT led to reductions in heart failure-related hospitalizations and urgent care visits among patients with heart failure and atrioventricular

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 a small RCT have suggested that biventricular pacing is associated with improvement in 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 and a meta-analysis that included nonrandomized studies. The relevant outcomes are OS, symptoms, functional outcomes, QOL, hospitalizations, and treatment-related morbidity. The available RCTs have reported improved outcomes on at least one measure of functional status or QOL with triple-site CRT compared with conventional CRT. However, the trials were small and had methodologic limitations. Also, 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 define better the benefit-risk ratio for triple-site CRT compared with 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. The relevant outcomes are OS, symptoms, functional outcomes, QOL, 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 ≤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 ≤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 ≤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.

Cardiac resynchronization therapy with wireless left ventricular endocardial pacing is considered **investigational.**

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

HEART FAILURE

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.

Treatment

Biventricular pacemakers using three leads (one in the right atrium, one endocardial in the right ventricle, one epicardial for the left ventricle), also known as cardiac resynchronization therapy (CRT), have been investigated as a technique to coordinate the contraction of the ventricles, thus improving patients' hemodynamic status. 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. Wireless left ventricular endocardial pacing is also being evaluated for patients who are not candidates for or do not respond to standard epicardial pacing leads.

REGULATORY STATUS

There are numerous CRT devices, combined implantable cardioverter defibrillator (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 New York Heart Association (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 left ventricular ejection fraction (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 CRT 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 the FDA for its combined ICD-D device with ventricular pacing leads (Tupos LV/ATx CRT-D/Kronos LV-T CRT-D systems[1]); in 2013, the company received the FDA approval for updated ICD-D devices (Ilesto/Iforia series).[2]

In September 2010, the FDA expanded indications for some CRT devices to include patients with class I and II heart failure. Based on data from the Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy study, indications for 3 Guidant CRT-D (Cognis®, Livian®, and Contak Renewal; Boston Scientific) 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 classifications[3]:

- 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 atrioventricular 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 the use of CRT in patients with NYHA class I, II, or III heart failure, LVEF of 50% or less, and atrioventricular 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 the FDA in August 2014. The Dynagen™ X4 and Inogen™ X4 devices (Boston Scientific) also incorporate a fourth lead. Other CRT devices with quadripolar leads have been approved for use outside of the U. S. (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 the 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.

The WiSE-CRT (EBR Systems) provides CRT with a small wireless electrode that is implanted within the left ventricle and controlled by ultrasound. It has European CE approval and is being studied in a multicenter pivotal trial.

FDA product code: NIK.

RELATED PROTOCOL

Implantable Cardioverter Defibrillator

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

REFERENCES

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

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