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FEP Medical Policy Manual

FEP 2.02.10 Biventricular Pacemakers (Cardiac Resynchronization Therapy) for the Treatment of Heart Failure

Effective Policy Date: October 1, 2022

Original Policy Date: December 2011

Related Policies:

7.01.44 - Implantable Cardioverter Defibrillators

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

Description

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).

OBJECTIVE

The objective of this evidence review is to determine whether cardiac resynchronization therapy improves the net health outcome in individuals with heart failure.

POLICY STATEMENT

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

For New York Heart Association class III or IV,

- Left ventricular ejection fraction ≤35%
- Sinus rhythm
- Individuals treated with guideline-directed medical therapy (see Policy Guidelines section)

AND

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

For New York Heart Association class II,

- Left ventricular ejection fraction ≤30%
- Sinus rhythm
- Individuals treated with a guideline-directed medical therapy (see Policy Guidelines section)

AND

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

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

- New York Heart Association 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 section); and
- Individuals treated with guideline-directed medical therapy (see Policy Guidelines section).

Biventricular pacemakers, with or without an accompanying implantable cardiac defibrillator (ie, a combined biventricular pacemaker plus implantable cardiac defibrillator), are considered **not medically necessary** as a treatment for individuals with New York Heart Association class I heart failure who do not meet the above criteria.

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

Triple-site (triventricular) cardiac resynchronization therapy, using an additional pacing lead, is considered **not medically necessary**.

An intrathoracic fluid monitoring sensor is considered **not medically necessary** as a component of a biventricular pacemaker.

Cardiac resynchronization therapy with wireless left ventricular endocardial pacing is considered **not medically necessary**.

POLICY GUIDELINES

Definitions

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

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

Guideline-directed medical therapy for heart failure is outlined in the 2022 American Heart Association, American College of Cardiology, and Heart Failure Society of America guidelines for the management of heart failure (Heidenreich et al [2022]).

BENEFIT APPLICATION

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

FDA 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 CRT-D device with ventricular pacing leads (Tupos LV/ATx CRT-D/Kronos LV-T CRT-D systems[4,]); in 2013, the company received the FDA approval for updated CRT-D devices (Ilesto/Iforia series).[5,]On the basis of the Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy (MADIT-CRT) 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[4,]:

- Moderate-to-severe heart failure (NYHA class III or 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 Biventricular versus Right Ventricular Pacing in Heart Failure Patients with Atrioventricular Block (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. (eg, 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. Evidence review 2.02.24 addresses the use of external bioimpedance devices as stand-alone devices to assess cardiac output noninvasively.

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.

RATIONALE

Summary of Evidence

For individuals who have NYHA class III or IV heart failure with an 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 cardiac resynchronization therapy (CRT) with or without defibrillator, the evidence includes randomized controlled trials (RCTs) and systematic reviews of RCTs. Relevant outcomes are OS, symptoms, functional outcomes, quality of life, 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 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 an improvement in the net health outcome.

For individuals who have NYHA class II heart failure with an 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 OS, symptoms, functional outcomes, quality of life, hospitalizations, and treatment-related morbidity. For patients with NYHA class II heart failure, at least 4 RCTs assessing CRT have been published. A mortality benefit was reported in 1 of the 4 trials, the RAFT trial. None of the other 3 RCTs reported a mortality difference, but a subgroup analysis of the Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy (MADIT-CRT) trial reported a mortality benefit for patients with LBBB. Among other outcome measures, hospitalizations for heart failure showed consistent reductions, but quality of life 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 an 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 (OS), 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 heart failure. While the treatment effect on death and hospitalization favored combined 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 that the technology results in an improvement in the net health outcome.

For individuals who have NYHA class I, II, III or IV heart failure with LVEF of 50% or less and AV nodal 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. Relevant outcomes are OS, symptoms, functional outcomes, quality of life, hospitalizations, and treatment-related morbidity. For patients who have atrioventricular (AV) nodal block, some degree of left ventricular (LV) 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 LV 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 an 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 6 RCTs and a registry study. Relevant outcomes are OS, symptoms, functional outcomes, quality of life, hospitalizations, and treatment-related morbidity. Results from RCTs have been conflicting, with 3 reporting improvements for patients with atrial fibrillation, including an all-cause mortality benefit, and others reporting no significant improvements. A registry study reported significant improvements in mortality and hospitalizations for patients with heart failure and atrial fibrillation treated with CRT plus defibrillator compared with implantable cardioverter-defibrillator alone. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have heart failure and AV nodal block who receive CRT, the evidence includes RCTs. Relevant outcomes are OS, symptoms, functional outcomes, quality of life, 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 AV block who would not necessarily meet conventional criteria for CRT. For patients who require ventricular pacing but have no LV 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 an 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. Relevant outcomes are OS, symptoms, functional outcomes, quality of life, hospitalizations, and treatment-related morbidity. The available RCTs have reported improved outcomes on at least 1 measure of functional status or quality of life 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 that the technology results in an improvement in the net health outcome.

For individuals who have heart failure who receive CRT combined with remote fluid monitoring, the evidence includes 3 RCTs. Relevant outcomes are OS, 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 that the technology results in an improvement in the net health outcome.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information" if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American College of Cardiology et al

The American College of Cardiology (ACC), American Heart Association, and Heart Rhythm Society (2019) published joint guidelines on the evaluation and management of patients with bradycardia and cardiac conduction delay.[89,] These guidelines included the following recommendations on CRT (see Table 1).

Table 1. Joint Guidelines on Treatment of Patients with Bradycardia and Cardiac Conduction Delay

Recommendation	COR	LOE
"In patients with atrioventricular block who have an indication for permanent pacing with a LVEF between 36% and 50% and are expected to require ventricular pacing more than 40% of the time, it is reasonable to choose pacing methods that maintain physiologic ventricular activation (e.g., cardiac resynchronization therapy [CRT] or His bundle pacing) over right ventricular pacing."	IIa	B-R[SR]
"In patients with atrioventricular block who have an indication for permanent pacing with a LVEF between 36% and 50% and are expected to require ventricular pacing less than 40% of the time, it is reasonable to choose right ventricular pacing over pacing methods that maintain physiologic ventricular activation (e.g., CRT or His bundle pacing)."	IIa	B-R

COR: class of recommendation; CRT: cardiac resynchronization therapy; LOE: level of evidence; LVEF: left ventricular ejection fraction; SR: systematic review.

A focused update to 2008 guidelines[90,] for device-based treatment of cardiac rhythm abnormalities was published jointly by ACC Foundation, American Heart Association, and Heart Rhythm Society in 2012.[91,]The ACC and American Heart Association (2013) subsequently published guidelines for the management of heart failure.[92,] These guidelines made recommendations on CRT for heart failure that are in line with those made by the ACC, American Heart Association, and Heart Rhythm Society related to CRT for heart failure in 2012. The ACC, American Heart Association,

and Heart Failure Society of America published guidelines on the management of heart failure (2022) to replace the 2013 guidelines.[93,]The most recent recommendations on CRT for heart failure from the guidelines are included in Table 2.

Table 2. Joint Guidelines on Device-Based Treatment of Cardiac Rhythm Abnormalities

Recommendation	COR	LOE
CRT is indicated for patients who have LVEF less than or equal to 35%, sinus rhythm, LBBB with a QRS duration greater than or equal to 150 ms, and NYHA class II, III, or ambulatory IV symptoms on GDMT	I	B[a]
CRT can be useful for patients who have LVEF less than or equal to 35%, sinus rhythm, LBBB with a QRS duration 120 to 149 ms, and NYHA class II, III, or ambulatory IV symptoms on GDMT	IIa	B[b]
CRT can be useful for patients who have LVEF less than or equal to 35%, sinus rhythm, a non-LBBB pattern with a QRS duration greater than or equal to 150 ms, and NYHA class II, III, or ambulatory class IV symptoms on GDMT	IIa	B[a]
CRT is reasonable in patients with high-degree or complete heart block and LVEF of 36% to 50%	IIa	B[a]
CRT can be useful in patients with atrial fibrillation and LVEF less than or equal to 35% on GDMT if a) the patient requires ventricular pacing or otherwise meets CRT criteria and b) AV nodal ablation or pharmacologic rate control will allow near 100% ventricular pacing with CRT	IIa	B[b]
CRT can be useful for patients on GDMT who have LVEF less than or equal to 35% and are undergoing new or replacement device placement with anticipated requirement for significant (>40%) ventricular pacing	IIa	B[b]
CRT may be considered for patients who have LVEF less than or equal to 30%, ischemic etiology of heart failure, sinus rhythm, LBBB with a QRS duration of greater than or equal to 150 ms, and NYHA class I symptoms on GDMT	IIb	B[b]
CRT may be considered for patients who have LVEF less than or equal to 35%, sinus rhythm, a non-LBBB pattern with QRS duration 120 to 149 ms, and NYHA class III/ambulatory class IV on GDMT	IIb	B[b]
CRT is not recommended in patients with QRS duration less than 120 ms	III[c]	B[a]
CRT is not recommended for patients with NYHA class I or II symptoms and non-LBBB pattern with QRS duration less than 150 ms	III[c]	B[b]
CRT-Dis not indicated for patients whose comorbidities and/or frailty limit survival with good functional capacity to less than 1 year	III[c]	C[d]

AV: atrioventricular; COR: class of recommendation; CRT: cardiac resynchronization therapy; CRT-D: cardiac resynchronization therapy with defibrillation; GDMT: guideline-directed medical therapy; LBBB: left bundle branch block; LOE: level of evidence; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association.

[a]Moderate quality evidence from 1 or more RCTs..

[b]Moderate-quality evidence from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies.

[c]No benefit.

[d]Limited data.

Heart Failure Society of America

The Heart Failure Society of America (2010) released comprehensive guidelines on the management of heart failure.[94,] The guidelines included the following recommendations on the use of CRT (see Table 3). The guidelines were updated in conjunction with the ACC and American Heart Association in 2022[93,] ; updated recommendations can be found above, in Table 3.

Table 3. Guidelines on Management of Heart Failure

Recommendation	LOE
Biventricular pacing therapy is recommended for patients in sinus rhythm with a widened QRS interval (≥120 ms) and severe LV systolic dysfunction (LVEF ≤35%) who have persistent, moderate to severe HF (NYHA III) despite optimal medical therapy.	A
Biventricular pacing therapy may be considered for patients with atrial fibrillation with a widened QRS interval (≥120 ms) and severe LV systolic dysfunction LVEF ≤35% who have persistent, moderate to severe HF (NYHA III) despite optimal medical therapy.	B
Selected ambulatory NYHA IV patients in sinus rhythm with QRS ≥120 ms and LV systolic dysfunction may be considered for biventricular pacing therapy.	B
Biventricular pacing therapy may be considered in patients with reduced LVEF and QRS ≥150 ms who have NYHA I or II HF symptoms.	B
In patients with reduced LVEF who require chronic pacing and in whom frequent ventricular pacing is expected, biventricular pacing may be considered.	C

HF: heart failure; LOE: level of evidence; LV: left ventricular; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association.

National Institute for Health and Care Excellence

The NICE (2014) guidance provided recommendations on CRT for heart failure.[95,] The recommendations for patients with left ventricular ejection fraction of 35% or less are listed in Table 4.

Table 4. Guidelines on Management of Cardiac Resynchronization Therapy for Heart Failure

Indication	Recommendation
NYHA class I-IV with QRS interval <120 ms	CRT not recommended
NYHA class IV with QRS interval 120 to 149 ms and without LBBB	CRT-P recommended
NYHA class II-III with QRS interval 120 to 149 ms and with LBBB	CRT-D recommended
NYHA class III-IV with QRS interval 120 to 149 ms and with LBBB	CRT-P recommended
NYHA class I-III with QRS interval ≥150 ms (with or without LBBB)	CRT-D recommended
NYHA class III-IV with QRS interval ≥150 ms (with or without LBBB)	CRT-P recommended

CRT: cardiac resynchronization therapy; CRT-D: cardiac resynchronization therapy with implantable cardioverter-defibrillator; CRT-P: cardiac resynchronization therapy with pacemaker; LBBB: left bundle branch block; NYHA: New York Heart Association.

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

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POLICY HISTORY - THIS POLICY WAS APPROVED BY THE FEP® PHARMACY AND MEDICAL POLICY COMMITTEE ACCORDING TO THE HISTORY BELOW:

Date	Action	Description
December 2011	New policy	
September 2013	Replace policy	Policy updated with literature review. Cardiac resynchronization therapy added to title. Numerous new references added, others reordered and/or removed. Cardiac resynchronization as treatment of heart failure in patients with atrial fibrillation is not medically necessary is added as a policy statement. Added investigational policy statement for triple-site (triventricular) CRT.
June 2014	Replace policy	Policy updated with literature review through March 6, 2014; references 11, 19, 25, 30, 31, 38, 41, 47, 49, 50, 51, 52, 53, added. Policy statements unchanged. Rationale reorganized and edited for clarity. Policy updated with literature review through March 6, 2014; references 11, 19, 25, 30, 31, 38, 41, 47, 49, 50, 51, 52, 53, added. Policy statements unchanged. Rationale reorganized and edited for clarity.
June 2015	Replace policy	Policy updated with literature review through March 11, 2015; references 1, 4, 11-12, 14, 30, 32-33, 49, 60, and 62 added. Policy statements for CRT in class II and II/IV heart failure changed to include presence of LBBB (and QRS >120- 130 ms) OR QRS >150 ms as medically necessary criteria. Policy statement added that CRT in patients with heart failure and AV block may be considered medically necessary with criteria.
June 2016	Replace policy	Policy updated with literature review through March 24, 2016. References 15, 51-53, 54-55, 57, and 60-61 added. No change to policy statements.
September 2018	Replace policy	Policy updated with literature review through March 5, 2018; References 5, 11, 14-38, 40-42, 44-46, 52, 65-67, 74, 78, 80, 90, 92, 98 added; reference 30 updated. Policy statement added that cardiac resynchronization therapy with wireless left ventricular endocardial pacing is considered not medically necessary.
September 2019	Replace policy	Policy updated with literature review through April 2, 2019; reference added. Policy statements unchanged.
September 2020	Replace policy	Policy updated with literature review through March 31, 2020; no references added. Policy statements unchanged.
September 2021	Replace policy	Policy updated with literature review through March 31, 2021; references added and updated. Policy statements unchanged.
September 2022	Replace policy	Policy updated with literature review through April 5, 2022; references added and updated. Minor editorial refinements to policy statements; intent unchanged.