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

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**Type of Submission – Check all that apply:**

- [ ] New Policy
- [x] Revised Policy*
- [ ] Annual Review – No Revisions
- [ ] Statewide PDL

*All revisions to the policy must be highlighted using track changes throughout the document.

Please provide any clarifying information for the policy below:

**CPB 0610 Biventricular Pacing (Cardiac Resynchronization Therapy)/Combination Resynchronization-Defibrillation Devices for Congestive Heart Failure**

Clinical content was last revised on 06/05/2018. Additional non-clinical updates were made by Corporate since the last PARP submission, as documented below.

**Update History since the last PARP Submission:**

01/27/2020-This CPB has been updated with additional references.

**Name of Authorized Individual (Please type or print):**

Benjamin Alouf, MD, MBA, FAAP

**Signature of Authorized Individual:**

[Signature]
Biventricular Pacing (Cardiac Resynchronization Therapy)/Combination Resynchronization-Defibrillation Devices for Congestive Heart Failure

Number: 0610

Policy

*Please see amendment for Pennsylvania Medicaid at the end of this CPB.*

I. Aetna considers Food and Drug Administration (FDA)-approved biventricular pacemakers (cardiac resynchronization therapy) medically necessary for the treatment of members with congestive heart failure (CHF) who are in sinus rhythm when either of the following criteria is met (A or B):

A. New York Heart Association (NYHA) classification of heart failure III or IV (see Appendix) and all of the following criteria are met:

1. Left ventricular ejection fraction (LVEF) less than or equal to 35%; and
2. QRS duration greater than or equal to 150 msec; 
and
3. Member is on an optimal pharmacologic regimen, 
defined as 3 months of maximally titrated doses 
as tolerated, before implantation, which may 
include any of the following, unless 
contraindicated:
   a. Angiotensin-converting enzyme inhibitor; or
   b. Angiotensin receptor blocker; or
   c. Beta blocker; or
   d. Digoxin; or
   e. Diuretics; or

4. Member is at least 40 days post myocardial 
   infarction (MI).

B. NYHA classification of heart failure II-IV (see 
Appendix) and all of the following criteria are met:

1. LVEF less than or equal to 35%; and
2. Left bundle branch block with QRS duration 
greater than or equal to 130 msec; and
3. Member is on an optimal pharmacologic regimen, 
defined as 3 months of maximally titrated doses 
as tolerated, before implantation, which may 
include any of the following, unless 
contraindicated.
   a. Angiotensin-converting enzyme inhibitor; or
   b. Angiotensin receptor blocker; or
   c. Beta blocker; or
   d. Digoxin; or
   e. Diuretics; or

4. Member is at least 40 days post MI.
II. Aetna considers biventricular pacemakers experimental and investigational for all other indications (e.g., atrial fibrillation, mild heart failure/NYHA functional class I, and anti-bradycardia pacing) because their effectiveness for these indications has not been established.

III. Aetna considers FDA-approved combination resynchronization-defibrillator devices medically necessary for members who are at high-risk for sudden cardiac death when the afore-mentioned criteria are fulfilled and any of the criteria listed below is met:

A. Members have at least 1 episode of cardiac arrest as a result of ventricular tachyarrhythmias; or
B. Members have recurring, poorly tolerated sustained ventricular tachycardia; or
C. Members have a prior heart attack and a documented episode of non-sustained ventricular tachycardia, with an inducible ventricular tachyarrhythmia; or
D. Members have a prior heart attack and a LVEF of less than or equal to 30%.

IV. Aetna considers combination resynchronization-defibrillator devices experimental and investigational for all other indications because their effectiveness for these indications has not been established.

V. Aetna considers cardiac resynchronization therapy with wireless left ventricular endocardial pacing for the treatment of heart failure experimental and investigational because the effectiveness of this approach has not been established.

VI. Aetna considers the galectin-3 test experimental and investigational for selection of individuals for cardiac resynchronization therapy and all other indications (e.g.,
prediction of outcome in individuals with stable dilated cardiomyopathy, prognosis of aortic valve stenosis/heart failure, risk prediction of atrial fibrillation) because its effectiveness has not been established.

Note: Biventricular pacemakers (cardiac resynchronization therapy) or combination resynchronization-defibrillator devices are not considered medically necessary for individuals whose heart failures or ventricular arrhythmias are reversible or temporary.

Contraindications

The following approaches are considered not medically necessary in persons with these contraindications:

- Asynchronous pacing is contraindicated in the presence (or likelihood) of competitive paced and intrinsic rhythms; or
- Unipolar pacing is contraindicated in individuals with an implanted defibrillator or cardioverter-defibrillator (ICD) because it may cause unwanted delivery or inhibition of defibrillator or ICD therapy.

See CPB 0585 - Cardioverter-Defibrillators also (../500_599/0585.html).

Background

Approximately 5 million Americans are currently diagnosed with heart failure (HF), and more than 500,000 new cases are diagnosed each year. Up to 50% of patients with advanced HF exhibit inter-ventricular conduction delay (ventricular dysynchrony), which result in abnormal contraction of the heart. Furthermore, prolonged QRS duration in these patients causes abnormal septal wall motion, reduced cardiac
contractility, decreased diastolic filling time and extended mitral regurgitation. These abnormalities have been reported to be associated with increased morbidity and mortality. Biventricular pacing has been examined as a technique to coordinate the contraction of the ventricles, thus improving the hemodynamic status of the patient. Two approaches are being studied: (i) incorporation of biventricular pacing into automatic implantable cardiac defibrillators; and (ii) development of stand-alone biventricular pacemakers.

Cardiac resynchronization therapy (CRT) refers to pacing techniques that alter the degree of atrial and ventricular electromechanical asynchrony in patients with severe atrial and ventricular conduction disorders. These devices provide electrical stimulation to both sides of the heart (left and right) thereby synchronizing atrioventricular contractions and coordinating (resynchronizing) ventricular contractions. Ventricular resynchronization has been shown to result in greater clinical value than atrial resynchronization.

Individuals with dyssynchrony (the right and left ventricles do not contract and empty simultaneously) and who are at risk for developing life threatening arrhythmias, may be considered for implantation of a cardiac resynchronization therapy/implantable cardioverter defibrillator (CRT-ICD), which provides the dual function of CRT and an implantable cardioverter defibrillator. The dual role allows for coordinating ventricular contractions and terminating life threatening arrhythmias.

In 1998, the American College of Cardiology and the American Heart Association issued a joint guideline for implantation of cardiac pacemakers and anti-arrhythmia devices. The joint guideline addressed New York Heart Association (NYHA) Class III and IV patients and stated that "Preliminary data suggest that simultaneous biventricular pacing may improve cardiac hemodynamics and lead to subjective and objective
symptom improvement”. Recent studies have reported that CRT with biventricular pacing to be beneficial for patients with congestive heart failure (CHF), improving both hemodynamic and clinical performance of these patients.

The InSync Biventricular Pacing System (Medtronic, Minneapolis, MN) is a stand-alone biventricular pacemaker that has been approved by the Food and Drug Administration (FDA) for the treatment of patients with NYHA Class III or IV heart failure, who are on a stable pharmacologic regimen, and who additionally have a QRS duration of greater than or equal to 130 msec and left ventricular ejection fraction (LVEF) of less than 35%.

The Guidant Cardiac Resynchronization Therapy Defibrillator System -- the CONTAK RENEWAL -- is a combination resynchronization-defibrillator device that has been approved by the FDA. It is indicated for patients who are at high-risk of sudden death due to ventricular arrhythmias and who have moderate-to-severe HF (NYHA Class III/IV) including left ventricular dysfunction (LVEF less than or equal to 35%) and QRS duration greater than or equal to 130 msec, and remain symptomatic despite stable, optimal heart failure drug therapy. Other combination resynchronization-defibrillator devices currently on the market include the Boston Scientific COGNIS and VIVIAN CRT with defibrillator (CRT-D) Systems, and the Medtronic InSync ICD Model 7272.

There is a lack of evidence that echocardiographic parameters can improve selection of patients for CRT. Chung and colleagues (2008) noted that data from single-center studies suggested that echocardiographic parameters of mechanical dyssynchrony may improve patient selection for CRT. In a prospective, multi-center setting, the Predictors of Response to CRT (PROSPECT) study, these researchers tested the performance of these parameters to predict CRT response. A total of 53 centers in Europe, Hong Kong, and the United States enrolled 498 patients with standard CRT indications.
(NYHA class III or IV heart failure, LVEF less than or equal to 35%, QRS greater than or equal to 130 ms, stable medical regimen). Twelve echocardiographic parameters of dyssynchrony, based on both conventional and tissue Doppler-based methods, were evaluated after site training in acquisition methods and blinded core laboratory analysis. Indicators of positive CRT response were improved clinical composite score and greater than or equal to 15% reduction in left ventricular end-systolic volume at 6 months. Clinical composite score was improved in 69% of 426 patients, whereas left ventricular end-systolic volume decreased greater than or equal to 15% in 56% of 286 patients with paired data. The ability of the 12 echocardiographic parameters to predict clinical composite score response varied widely, with sensitivity ranging from 6% to 74% and specificity ranging from 35% to 91%; for predicting left ventricular end-systolic volume response, sensitivity ranged from 9% to 77% and specificity from 31% to 93%. For all the parameters, the area under the receiver-operating characteristics curve for positive clinical or volume response to CRT was less than or equal to 0.62. There was large variability in the analysis of the dyssynchrony parameters. The authors concluded that given the modest sensitivity and specificity in this multi-center setting despite training and central analysis, no single echocardiographic measure of dyssynchrony may be recommended to improve patient selection for CRT beyond current guidelines.

Anderson et al (2008) reviewed the status of proposed dyssynchrony indexes by echocardiography for patient selection in CRT. The authors concluded that despite the huge output of publications in this field, they do not presently advise incorporating echocardiographic dyssynchrony parameters for the selection of candidates for CRT for the following reasons: (i) no large published clinical trials exist to demonstrate benefit with a particular dyssynchrony index, (ii) conflicting results are emerging on the predictive value
of dyssynchrony indexes, (iii) all the parameters described to date have either technical or theoretical limitations. A practical parameter or index for selection of appropriate patients for CRT should be simple and preferably should not require offline analysis. Clinically, it will be more important to identify non-responders to CRT using various clinical, laboratory, and echocardiographic data with a very high accuracy. This ideal parameter has not been found.

Hawkins et al (2009) stated that international guidelines unanimously endorse QRS prolongation to identify candidates for CRT, based on over 4,000 patients randomized in landmark trials. Small, observational, non-randomized studies with surrogate end points have promoted echocardiography as a superior method of patient selection. Over 30 dyssynchrony parameters have been proposed. Most lack validation in appropriate clinical settings, including demonstration of short-term as well as long-term reproducibility and intra- and inter-observer variability. Prospective multi-center trials have proved informative in unexpected ways. In core laboratories, parameters exhibit striking variability, poor reproducibility, and limited predictive power. The authors are concerned that many centers today are using these techniques to select patients for CRT. Publication density and bias have misinformed clinical decision making. These investigators stated that echocardiographic parameters have no place in denying potentially life-saving treatment or in exposing patients to unnecessary risks and draining health care resources. Such measures should not stray beyond the research environment unless validated in randomized trials with robust clinical end points. The electrocardiogram remains a simple, inexpensive, and reproducible tool that identifies patients likely to benefit from CRT. Patient selection must use the parameter prospectively validated in landmark clinical trials: the QRS duration.
Sanderson (2009) noted that after the publication of the PROSPECT trial, the use of echocardiography for the assessment of mechanical dyssynchrony and as a possible aid for selecting patients for CRT has been heavily criticized. Calls have been made to observe the current guidelines and implant according to the entry criteria of recent major trials. However, although this approach is currently to be recommended, the attempt to identify patients who will not receive the benefits of CRT and whose clinical condition may be worsened should continue. Professional resources and the costs to society are high and wasted if devices are implanted inappropriately; further work is needed to refine the techniques and new clinical trials performed. A combination of methods that include finding the site of latest mechanical activation, myocardial scar localization, and assessing venous anatomy pre-operatively may help to identify those who will not derive any benefit or be potentially worsened.

Stellbrink (2009) stated that CRT aims to correct the mechanical dyssynchrony in patients with heart failure and broad QRS complex. Until now, indication for CRT is based mainly on clinical and electrocardiographic criteria. Because QRS width is only weakly correlated to mechanical dyssynchrony, imaging techniques such as echocardiography and magnetic resonance tomography (MRT) seem suitable for analysis of dyssynchrony. Echocardiography has been studied in several studies for identification of suitable CRT candidates. Apart from conventional methods such as M mode-, 2 dimensional-, and Doppler-echocardiography, other techniques such as tissue Doppler echocardiography, have been used. Despite many positive results in individual studies no single echocardiographic parameter was able to predict positive CRT response in a prospective multi-center trial. Thus, QRS width remains the "gold standard" for CRT patient identification at present.
In a prospective, double-blind, multi-center study, Yu and associates (2009) examined if biventricular pacing is superior to right ventricular apical pacing in preventing deterioration of LV systolic function and cardiac remodeling in patients with bradycardia and a normal LVEF. These investigators randomly assigned 177 patients in whom a biventricular pacemaker had been successfully implanted to receive biventricular pacing (n = 89) or right ventricular apical pacing (n = 88). The primary end points were LVEF and left ventricular end-systolic volume (LVESV) at 12 months. At 12 months, the mean LVEF was significantly lower in the right-ventricular-pacing group than in the biventricular-pacing group (54.8 +/- 9.1 % versus 62.2 +/- 7.0 %, p < 0.001), with an absolute difference of 7.4 percentage points, whereas the LVESV was significantly higher in the right-ventricular-pacing group than in the biventricular-pacing group (35.7 +/- 16.3 ml versus 27.6 +/- 10.4 ml, p < 0.001), with a relative difference between the groups in the change from baseline of 25 % (p < 0.001). The deleterious effect of right ventricular apical pacing occurred in pre-specified subgroups, including patients with and patients without pre-existing LV diastolic dysfunction. Eight patients in the right-ventricular-pacing group (9 %) and 1 in the biventricular-pacing group (1 %) had LVEF of less than 45 % (p = 0.02). There was 1 death in the right-ventricular-pacing group, and 6 patients in the right-ventricular-pacing group and 5 in the biventricular-pacing group were hospitalized for HF (p = 0.74). The authors concluded that in patients with normal systolic function, conventional right ventricular apical pacing resulted in adverse LV remodeling and in a reduction in LVEF; these effects were prevented by biventricular pacing. Moreover, the authors stated that randomized trials with longer follow-up periods, larger samples, and sufficient power to assess clinical outcomes between these two pacing strategies are needed.

Daubert et al (2009) examined the long-term effects of CRT in the European cohort of patients enrolled in the REVERSE (Resynchronization Reverses Remodeling in Systolic Left
Ventricular Dysfunction) trial. These researchers randomly assigned 262 recipients of CRT pacemakers or defibrillators, with QRS greater than or equal to 120 ms and LVEF less than or equal to 40% to active (CRT ON; n = 180) versus control (CRT OFF; n = 82) treatment, for 24 months. Mean baseline LVEF was 28.0%. All patients were in sinus rhythm and receiving optimal medical therapy. The primary study end point was the proportion worsened by the heart failure (HF) clinical composite response. The main secondary study end point was LVESV index (LVESVi). In the CRT ON group, 19% of patients were worsened versus 34% in the CRT OFF group (p = 0.01). The LVESVi decreased by a mean of 27.5 +/- 31.8 ml/m(2) in the CRT ON group versus 2.7 +/- 25.8 ml/m(2) in the CRT OFF group (p < 0.0001). Time to first HF hospital stay or death (hazard ratio: 0.38; p = 0.003) was significantly delayed by CRT. The authors concluded that after 24 months of CRT, and compared with those of control subjects, clinical outcomes and LV function were improved and LV dimensions were decreased in this patient population in NYHA functional classes I or II. These findings suggested that CRT prevents the progression of disease in patients with asymptomatic or mildly symptomatic LV dysfunction.

In an editorial that accompanied the afore-mentioned article, Exner (2009) noted that the REVERSE trial demonstrated a 29% reduction in the risk of the combined end point of death or HF events (p = 0.003). This outcome was purely driven by a reduction in HF events. The proportion of these events that were actual hospitalizations for HF is unclear. Furthermore, the average 6-min walk test distance of 361 +/- 108 m suggested that many of these patients would have been categorized as NYHA functional class III in past trials, based on a walk distance of less than 450 m. The author stated that it is premature to recommend CRT as a routine intervention to patients with asymptomatic LV dysfunction or those with mildly symptomatic HF today.
In September 2010, the FDA approved a new indication for 3 cardiac resynchronization therapy defibrillators (CRT-D) used to treat certain heart failure patients. The new use is for patients with left bundle branch block, which occurs when there is delayed activation and contraction of the left ventricle. The 3 devices, all manufactured by Boston Scientific Corp., are intended to treat patients with left bundle branch block who have either mild heart failure or heart failure with no apparent symptoms. CRT-Ds are to be used as an addition to, not a replacement for, heart failure drug therapy. The FDA based its approval on the results of the 1,820-patient Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy (MADIT-CRT) clinical study. The study, which followed 1,820 patients for an average of nearly 3 years at 110 centers in the Canada, Europe, Israel, and United States. It compared CRT-D therapy to implantable cardioverter-defibrillator (ICD)-only therapy in specific heart failure patients to determine whether it reduced the risk of death and heart failure. In patients with left bundle branch block, who represented 70% of the study group, CRT-D showed a reduction in the risk of death and heart failure by 57%, as compared to ICD alone. The rate of complications was considered to be acceptable by the FDA for this device, however, physicians should adequately inform patients about potential complications.

As a condition of FDA approval, Boston Scientific must conduct 2 post-approval studies. One study will evaluate complications and long-term mortality benefits of CRT-D in patients with left bundle branch block identified through the National Cardiovascular Data Registry. The other will follow patients from the original MADIT-CRT clinical study every 6 months for 5 years to assess long-term mortality benefits of CRT-D versus ICD.

The efficacy of CRT in patients with mild or moderate HF was confirmed by the Resynchronization–Defibrillation for Ambulatory Heart Failure Trial (RAFT trial). Tang, et al (2010)
reported on a controlled clinical study that found that, among patients with NYHA class II or III heart failure, a wide QRS complex, and left ventricular systolic dysfunction, the addition of CRT to an ICD reduced rates of death and hospitalization for heart failure. The investigators randomly assigned 1,798 patients with NYHA class II or III HF, a LVEF of 30 % or less, and an intrinsic QRS duration of 120 msec or more or a paced QRS duration of 200 msec or more to receive either an ICD alone or an ICD plus CRT. The primary outcome was death from any cause or hospitalization for HF, and subjects were followed for a mean of 40 months. The primary outcome occurred in 297 of 894 patients (33.2 %) in the ICD–CRT group and 364 of 904 patients (40.3 %) in the ICD group (hazard ratio in the ICD–CRT group, 0.75; 95 % confidence interval [CI]: 0.64 to 0.87; p < 0.001). In the ICD–CRT group, 186 patients died, as compared with 236 in the ICD group (hazard ratio, 0.75; 95 % CI: 0.62 to 0.91; p = 0.003), and 174 patients were hospitalized for HF, as compared with 236 in the ICD group (hazard ratio, 0.68; 95 % CI: 0.56 to 0.83; p < 0.001). However, at 30 days after device implantation, adverse events had occurred in 124 patients in the ICD-CRT group, as compared with 58 in the ICD group (p < 0.001).

An assessment by the BlueCross BlueShield Association (BCBSA, 2011) Technology Evaluation Center (TEC) of cardiac resynchronization therapy for mild HF concluded that the use of cardiac resynchronization therapy for mild heart failure meets the TEC criteria for persons with NYHA class II heart failure who have a LVEF less than 30% and a QRS duration of greater than or equal to 130 msec. The use of cardiac resynchronization therapy for mild HF in other patient populations (e.g., NYHA class I HF) did not meet TEC criteria.

In a review on CRT in patients with NYHA class I and II HF, Linde and Daubert (2010) stated that a wider use of CRT in mildly symptomatic patients to prevent disease progression needs to be considered in the near future. First, however,
whether mortality is influenced by CRT needs to be clarified, as well as the balance between the risks of CRT treatment and the potential benefits.

van Bommel et al (2011) noted that functional mitral regurgitation (MR) is a common finding in HF patients with dilated cardiomyopathy and has important prognostic implications. However, the increased operative risk of these patients may result in low-referral or high-denial rate for mitral valve surgery. Cardiac resynchronization therapy has been shown to have a favorable effect on MR. The aims of this study were to (i) evaluate CRT as a therapeutic option in HF patients with functional MR and high operative risk, and (ii) examine the effect of MR improvement after CRT on prognosis. A total of 98 consecutive patients with moderate-severe functional MR and high operative risk underwent CRT according to current guidelines. Echocardiography was performed at baseline and 6-month follow-up; severity of MR was graded according to a multi-parametric approach. Significant improvement of MR was defined as a reduction greater than or equal to 1 grade. All-cause mortality was assessed during follow-up (median of 32 [range of 6.0 to 116] months). Thirteen patients (13 %) died before 6-months follow-up. In the remaining 85 patients, significant reduction in MR was observed in all evaluated parameters. In particular, 42 patients (49 %) improved greater than or equal to 1 grade of MR and were considered MR improvers. Survival was superior in MR improvers compared to MR non-improvers (log rank p < 0.001). Mitral regurgitation improvement was an independent prognostic factor for survival (hazard ratio 0.35, CI: 0.13 to 0.94; p = 0.043). The authors concluded that CRT is a potential therapeutic option in HF patients with moderate-severe functional MR and high-risk for surgery. Improvement in MR results in superior survival after CRT.
Stavrakis et al (2012) stated that atrio-ventricular junction (AVJ) ablation with permanent pacing improves symptoms in selected patients with atrial fibrillation (AF). The optimal pacing modality after AVJ ablation remains unclear. In a meta-analysis, these investigators examined if CRT is superior to right ventricular (RV) pacing in this patient population. They searched the MEDLINE and EMBASE databases for studies evaluating the effect of CRT versus RV pacing after AVJ ablation for AF. Pooled risk ratios (RRs) and mean differences with 95% CIs were calculated for categorical and continuous outcomes, respectively, using a random effects model. A total of 5 trials involving 686 patients (413 in CRT and 273 in RV pacing group) were included in the analysis. On the basis of the pooled estimate across the studies, CRT resulted in a non-significant reduction in mortality (RR = 0.75, 95% CI: 0.43 to 1.30; p = 0.30) and a significant reduction in hospitalizations for heart failure (RR = 0.38, 95% CI: 0.17 to 0.85; p = 0.02) compared with RV pacing. Cardiac resynchronization therapy did not improve 6-min walk distance (mean difference 15.7, 95% CI: -7.2 to 38.5 m; p = 0.18) and Minnesota Living with Heart Failure quality-of-life score (mean difference -3.0, 95% CI: -8.6 to 2.6; p = 0.30) compared with RV pacing. The change in LVEF between baseline and 6 months favored CRT (mean change 2.0%, 95% CI: 1.5 to 2.4%; p < 0.001). The authors concluded that CRT may be superior to RV pacing in patients undergoing AVJ ablation for AF. Moreover, they stated that further studies, adequately powered to detect clinical outcomes, are needed.

Curtis et al (2013) noted that RV pacing restores an adequate heart rate in patients with AV block, but high percentages of RV apical pacing may promote left ventricular systolic dysfunction. These researchers examined if biventricular pacing might reduce mortality, morbidity, and adverse left ventricular re-modeling in such patients. They enrolled patients who had indications for pacing with AV block; NYHA class I, II, or III HF; and a LVEF of 50% or less. Patients received a cardiac-resynchronization pacemaker or ICD (the
latter if the patient had an indication for defibrillation therapy) and were randomly assigned to standard RV pacing or biventricular pacing. The primary outcome was the time to death from any cause, an urgent care visit for HF that required intravenous therapy, or a 15% or more increase in the left ventricular end-systolic volume index. Of 918 patients enrolled, 691 underwent randomization and were followed for an average of 37 months. The primary outcome occurred in 190 of 342 patients (55.6%) in the RV-pacing group, as compared with 160 of 349 (45.8%) in the biventricular-pacing group. Patients randomly assigned to biventricular pacing had a significantly lower incidence of the primary outcome over time than did those assigned to RV pacing (hazard ratio, 0.74; 95% CI: 0.60 to 0.90); results were similar in the pacemaker and ICD groups. Left ventricular lead-related complications occurred in 6.4% of patients. The authors concluded that biventricular pacing was superior to conventional RV pacing in patients with AV block and left ventricular systolic dysfunction with NYHA class I, II, or III HF.

Coburn and Frishman (2014) stated that HF is a major cause of morbidity and mortality in the United States; however, reliable biomarkers predicting outcomes of patients suffering from HF are still not available. Finding a prognostic indicator in patients with HF could ultimately help improve the quality of goal-directed care for these patients. A number of recent studies suggested that galectin-3, a peptide that has been repeatedly shown to be elevated in the setting of inflammatory processes, may provide information regarding the pathophysiologic process underlying HF. If this is the case, galectin-3 may independently be able to provide more information regarding prognosis in patients with HF than some of the more conventional indicators currently in use today (i.e., natriuretic peptide, C-reactive protein [CRP]). These researchers analyzed the most recent and comprehensive studies that have looked at the utility of galectin-3 as a prognostic marker in patients with HF. After a thorough review, they found that the evidence against the use of
galectin-3 as a prognostic biomarker in HF was too strong to support its routine use in current clinical settings. However, many of the studies, both in support of and in opposition to the prognostic potential of galectin-3, were uniformly limited by undersized cohorts, and thus the need for further exploration is clearly warranted.

Atabakhshian et al (2014) examined the relationship between galectin-3 as a biomarker and ejection fraction and functional capacity in the patients with compensated systolic HF. In this study, serum levels of galectin-3 were measured in 76 patients with compensated HF with NYHA class I to IV and LVEF less than 45 %. Galectin-3 was measured by an ELISA kit. Besides, echocardiography was used to evaluate LVEF. Additionally, functional capacity was determined based on the patients’ ability to perform a set of activities. After all, the data were analyzed using t-test, Kruskal-Wallis, 1-way ANOVA, and chi-square test; p < 0.05 was considered as statistically significant. The patients’ age ranged from 45 to 75 years, with the mean age of 63.85 ± 9 years. In addition, 57.9 % of the patients were male. The results revealed no significant correlation between galectin-3 and age, body mass index, and estimated glomerular filtration rate (eGFR). Also, no significant correlation was observed between galectin-3 levels and LVEF (p = 0.166) and functional capacity (p = 0.420). Yet, a significant difference was found between males and females regarding the mean of galectin-3 (p = 0.039). The authors concluded that the findings of this study suggested that galectin-3 could not be used as a marker of disease progression in the patients under treatment, which could probably be the result of medication use in these patients.

Srivatsan et al (2015) noted that HF continues to be an illness of daunting proportions with a 4-year mortality touching 50 %. Biomarkers for prognosticating patients with HF have generated immense interest. Several studies have been conducted on a novel biomarker, galectin-3 to assess its prognostic effect in HF populations. However, the studies
have generated conflicting results. These investigators performed a systematic review to assess the utility of galectin-3 as a prognostic biomarker in HF. They carried out a literature search using terms “galectin-3 and heart” and “galectin-3 and heart failure” in Medline, Science Direct, Scopus, Springer Link, Cochrane Library and Google Scholar for original articles using a predefined inclusion/exclusion criteria. A total of 27 original articles were selected for the systematic review. Multi-variate analysis showed galectin-3 to be ineffective in predicting all-cause mortality and cardiovascular mortality especially under the influence of factors such as eGFR, LVEF, and N-terminal fragment of B-type natriuretic peptide (NT-proBNP). Galectin-3 was not found to be superior to NT-proBNP, serum levels of soluble ST2 (sST2), GDF-15 or CRP as a predictor of mortality. However the combination of natriuretic peptides and galectin-3 has been observed to be superior in predicting mortality compared to either of the biomarkers alone. The role of galectin-3 in re-modelling has not been conclusively proven as seen in earlier pre-clinical studies. The authors concluded that the current weight of evidence does not suggest galectin-3 to be a predictor of mortality. However, assessment of galectin-3 in a multi-biomarker panel may have a distinct advantage in prognosticating patients with HF.

Shah and colleagues (2015) stated that CRT reduces morbidity and mortality in patients with chronic systolic HF (SHF) and a wide QRS complex. It is unclear whether the same benefit extends to patients with QRS duration (QRSd) of less than 130 ms. These investigators performed a meta-analysis of all randomized controlled trials (RCTs) and evaluated the effect of implantable CRT defibrillator (CRTD) on all-cause mortality, HF mortality, and HF hospitalization in patients with QRSd of less than 130 ms. They performed a systematic literature search to identify all RCTs, comparing CRTD therapy with ICD therapy in patients with SHF (EF less than 35 %) and QRS less than or equal to 130 ms, published in PubMed, Medline, Embase, Cochrane library, and Google
The search terms included CRT, QRS duration, narrow QRS, clinical trial, RCT, biventricular pacing, heart failure, systolic dysfunction, dyssynchrony, left ventricular remodeling, readmission, mortality, survival, and various combinations of these terms. The authors studied the trends of overall mortality, SHF mortality, and hospitalizations due to SHF between the 2 groups. Heterogeneity of the studies was analyzed by Q statistic. A fixed-effect model was used to compute the RR of mortality due to SHF, while a random-effects model was used to compare hospitalization due to SHF. Out of a total of 12,100 citations, 4 RCTs comparing CRTD versus ICD therapy in patients with SHF and QRS of less than or equal to 130 ms fulfilled the inclusion criteria. The median follow-up was 12 months and the cumulative number of patients was 1,177.

Relative risk for all-cause mortality in patients treated with CRTD was 1.66 with a 95% CI of 1.096 to 2.515 (p = 0.017) while for SHF mortality was 1.29 with 95% CI of 0.68 to 2.45 (p = 0.42). Relative risk for HF hospitalization in patients treated with CRTD was 0.94 with 95% CI of 0.50 to 1.74 (p = 0.84) in comparison to the ICD group. The authors concluded that CRT defibrillator has no impact on SHF mortality and SHF hospitalization in patients with systolic HF with QRS duration of less than or equal to 130 ms and is associated with higher all-cause mortality in comparison with ICD therapy.

Friedman and associates (2015) noted that patients with moderate-to-severe chronic kidney disease (CKD) are poorly represented in clinical trials of CRT. These researchers evaluated the real-world comparative effectiveness of CRT-D versus ICD alone in CRT-eligible patients with moderate-to-severe CKD. These investigators conducted an inverse probability-weighted analysis of 10,946 CRT-eligible patients (EF less than 35%, QRS greater than 120 ms, NYHA functional class III/IV) with stage 3 to 5 CKD in the National Cardiovascular Data Registry (NCDR) ICD Registry, comparing outcomes between patients who received CRT-D (n = 9,525) versus ICD only (n = 1,421). Outcomes were
obtained via Medicare claims and censored at 3 years. The primary end-point of HF hospitalization or death and the secondary end-point of death were assessed with Cox proportional hazards models; HF hospitalization, device explant, and progression to end-stage renal disease were assessed using Fine-Gray models. After risk adjustment, CRT-D use was associated with a reduction in HF hospitalization or death (hazard ratio [HR]: 0.84; 95 % CI: 0.78 to 0.91; p < 0.0001), death (HR: 0.85; 95 % CI: 0.77 to 0.93; p < 0.0004), and HF hospitalization alone (sub-distribution HR: 0.84; 95 % CI: 0.76 to 0.93; p < 0.009). Sub-group analyses suggested that CRT was associated with a reduced risk of HF hospitalization and death across CKD classes. The incidence of in-hospital, short-term, and mid-term device-related complications did not vary across CKD stages. The authors concluded that in a nationally representative population of HF and CRT-eligible patients, use of CRT-D was associated with a significantly lower risk of the composite end-point of HF hospitalization or death among patients with moderate-to-severe CKD in the setting of acceptable complication rates.

Rickard and colleagues (2016) determined predictors of response to CRT-D and CRT with pacemaker (CRT-P) utilizing the methods of systematic review. These investigators searched Medline, Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL) from January 1, 1995, as this is the date of first article reporting use of CRT through October 20, 2014. Paired investigators independently screened search results to assess eligibility. For inclusion, investigators abstracted data sequentially and assessed risk of bias independently. Investigators graded the strength of evidence as a group. They identified 13,015 unique citations of which 11,897 were excluded during the abstract screen. During the full-text screening, these researchers excluded 1,118 citations. 12 studies reported in 15 articles were included in this review. A left bundle branch (LBBB) morphology, non-ischemic cardiomyopathy (NICM), and female gender were generally associated with improved
outcomes following CRT-D. Sinus rhythm (as compared to AF) and a wider QRS duration were associated with improved outcomes following CRT-D albeit with a lower strength of evidence. There was insufficient evidence to determine predictors of outcomes in patients undergoing CRT-P. The authors concluded that a native LBBB, NICM, female gender, sinus rhythm, and a wider QRS duration are associated with improved outcomes following CRT-D implant.

2012 ACCF/AHA/HRS focused update was incorporated into the 2008 guidelines for device-based therapy of cardiac rhythm abnormalities. This guideline outlines indications for cardiac resynchronization therapy:

- CRT can be useful for persons 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 III/ambulatory class IV with symptoms on GDMT (LOE: A). (Note: the 2012 ACC/AHA/HRS guideline changed the QRS duration from 120 ms (2008 ACC/AHA/HRS guideline) to 150 ms).
- CRT is indicated for persons 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, and symptoms on while on guideline-directed medical therapy (GDMT) (LOE: A for NYHA class III/IV, LOE: B for NYHA class II).
- CRT can be useful for persons 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 with symptoms on GDMT (LOE: B).
- CRT is not recommended for patients with NYHA class I or II symptoms and non-LBBB pattern with QRS duration less than 150 ms (LOE: B).
An UpToDate review on “Cardiac resynchronization therapy in heart failure: Indications” (Adelstein and Saba, 2017) make the following CRT indication recommendations, which include persons who are in sinus rhythm and have an LVEF less than or equal to 35 percent, have optimal evidence-based medical therapy for at least three months after initial diagnosis (or for at least 40 days after myocardial infarction) and after treatment of any reversible causes of persistent HF, in addition to the following:

- QRS greater than or equal to 150 ms with LBBB and NYHA class II to ambulatory IV heart failure (HF); or
- QRS 130-149 ms with LBBB and NYHA class II to ambulatory class IV HF; or
- QRS greater than or equal to 150 ms with non-LBBB and NYHA class II or ambulatory IV HF.

In a meta-analysis, which included early crossover and 14 randomized trials with 4420 patients (nearly all with NYHA class III or IV symptoms, mean QRS range 155 to 209 ms), CRT increased the likelihood of improving by at least one NYHA class (59 versus 37 percent, RR 1.6, 95% CI 1.3-1.9). Hospitalizations for HF were reduced 37 percent, and all-cause mortality was reduced 22 percent, primarily because of a lower risk of HF-related death (RR 0.64, 95% CI 0.49-0.84) (Adelstein and Saba, 2017).

The Centers for Medicare & Medicaid Services (CMS) (2018) NCD decision memo for implantable cardioverter defibrillators states that while they reference CRT defibrillator devices in the document, there is no coverage determination made in an NCD. CRT devices are currently addressed by local Medicare contractors (LCD).

Cardiac Resynchronization Therapy plus Defibrillator for Patients with Mild Heart Failure
Biton and co-workers (2016) evaluated the long-term clinical outcomes of 537 non-LBB block patients with mild HF enrolled in the Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy (MADIT-CRT) study by QRS duration or morphology further stratified by PR interval. At 7 years of follow-up, the cumulative probability of HF hospitalization or death was 45 % versus 56 % among patients randomized to ICD and CRT-D, respectively (p = 0.209).

Multivariable-adjusted subgroup analysis by QRS duration showed that patients from the lower quartile QRS duration group (less than or equal to 134 ms) experienced 2.4-fold (p = 0.015) increased risk for HF hospitalization or death with CRT-D versus ICD only therapy, whereas the effect of CRT-D in patients from the upper quartiles group (QRS greater than 134 ms) was neutral (H] =0.97, p = 0.86; p value for interaction = 0.024). In a second analysis incorporating PR interval (time from the onset of the P wave to the start of the QRS complex), patients with prolonged QRS (greater than 134 ms) and prolonged PR (greater than 230 ms) were protected with CRT-D (HR = 0.31, p = 0.003), whereas the association was neutral with prolonged QRS (greater than 134 ms) and shorter PR (less than or equal to 230 ms; HR= 1.19, p = 0.386; p value for interaction = 0.002). The effect was neutral, regardless of morphology, right bundle branch block (HR = 1.01, p = 0.975), and intra-ventricular conduction delay (HR = 1.31, p = 0.172). The authors concluded that patients with mild HF but without LBB block morphology did not derive clinical benefit with CRT-D during long-term follow-up; relatively shorter QRS was associated with a significantly increased risk with CRT-D relative to ICD only.

Sun and associates (2016) noted that previous studies of CRT-D therapy used for primary prevention of sudden cardiac death have suggested that CRT-D therapy is less effective in patients with mild HF and a wide QRS complex. However, the long-term benefits are variable. These researchers performed a meta-analysis of randomized trials identified in systematic searches of Medline, Embase, and the Cochrane Database. A
total of 3 studies (3,858 patients) with a mean follow-up of 66 months were included. Overall, CRT-D therapy was associated with significantly lower all-cause mortality than was ICD therapy (OR, 0.78; 95% CI: 0.63 to 0.96; p = 0.02; I² = 19%). However, the risk of cardiac mortality was comparable between 2 groups (OR, 0.74; 95% CI: 0.53 to 1.01; p = 0.06). CRT-D treatment was associated with a significantly lower risk of hospitalization for HF (OR, 0.67; 95% CI: 0.50 to 0.89; p = 0.005; I² = 55%). The composite outcome of all-cause mortality and hospitalization for HF was also markedly lower with CRT-D therapy than with ICD treatment alone (OR, 0.67; 95% CI: 0.57 to 0.77; p < 0.0001; I² = 0%). The authors concluded that CRT-D therapy decreased the long-term risk of mortality and HF events in patients with mild HF with a wide QRS complex. However, long-term risk of cardiac mortality was similar between 2 groups. They stated that more randomized studies are needed to confirm these findings, especially in patients with NYHA class I HF or patients without LBBB.

Cardiac Resynchronization Therapy for the Treatment of Atrial Fibrillation

Gianni and colleagues (2017) stated that although CRT is an important treatment of symptomatic HF patients in sinus rhythm with low LVEF and ventricular dyssynchrony, its role is not well-defined in patients with AF. The authors stated that CRT is not as effective in patients with AF because of inadequate biventricular capture and loss of AV synchrony. Both can be addressed with catheter ablation of AF. It is still unclear if these therapies offer additive benefits in patients with ventricular dyssynchrony.

Cardiac Resynchronization Therapy with Wireless Left Ventricular Endocardial Pacing for the Treatment of Heart Failure
Reddy and colleagues (2017) noted that a total of 30% to 40% of patients with CHF eligible for CRT either do not respond to conventional CRT or remain untreated due to an inability or impediment to coronary sinus (CS) lead implantation. The WiSE-CRT system (EBR Systems, Sunnyvale, CA) was developed to address this at-risk patient population by performing bi-ventricular pacing via a wireless LV endocardial pacing electrode. The SELECT-LV (Safety and Performance of Electrodes implanted in the Left Ventricle) study is a prospective, multi-center, non-randomized trial evaluating the safety and effectiveness of the WiSE-CRT system. A total of 35 patients indicated for CRT who had “failed” conventional CRT underwent implantation of an LV endocardial pacing electrode and a subcutaneous pulse generator. System performance, clinical efficacy, and safety events were assessed out to 6 months post-implant. The procedure was successful in 97.1% (n = 34) of attempted implants. The most common indications for endocardial LV pacing were difficult CS anatomy (n = 12), failure to respond to conventional CRT (n = 10), and a high CS pacing threshold or phrenic nerve capture (n = 5). The primary performance end-point, bi-ventricular pacing on the 12-lead electrocardiogram (EKG) at 1 month, was achieved in 33 of 34 patients. A total of 28 patients (84.8%) had improvement in the clinical composite score at 6 months, and 21 (66%) demonstrated a positive echocardiographic CRT response (greater than or equal to 5% absolute increase in LVEF). There were no peri-cardial effusions, but serious procedure/device-related events occurred in 3 patients (8.6%) within 24 hours, and 8 patients (22.9%) between 24 hours and 1 month. The authors concluded that the SELECT-LV study demonstrated the clinical feasibility of the WiSE-CRT system, and provided clinical benefits to a majority of patients within an otherwise “failed” CRT population. This clinical trial is still ongoing, but not recruiting subjects (Last updated September 27, 2016).

Prognosis of Aortic Valve Stenosis
Arangalage and colleagues (2016) stated that myocardial fibrosis has been proposed as an outcome predictor in asymptomatic patients with severe aortic stenosis (AS) that may lead to consider prophylactic surgery. It can be detected using MRI but its widespread use is limited and development of substitute biomarkers is highly desirable. These researchers analyzed the determinants and prognostic value of galectin-3, one promising biomarker linked to myocardial fibrosis. Patients with at least mild degenerative AS enrolled between 2006 and 2013 in 2 ongoing studies, COFRASA/GENERAC (COhorte Française de Rétrécissement Aortique du Sujet Agé/GENEtique du Rétrécissement Aortique), aiming at assessing the determinants of AS occurrence and progression, constituted the study population. These investigators prospectively enrolled 583 patients. The mean galectin-3 value was 14.3 ± 5.6 ng/ml. There was no association between galectin-3 and functional status (p = 0.55) or AS severity (p = 0.58). Independent determinants of galectin-3 were age (p = 0.0008), female gender (p = 0.04), hypertension (p = 0.002), diabetes (p = 0.02), reduced LVEF (p = 0.01), diastolic dysfunction (E/e', p = 0.02) and creatinine clearance (p < 0.0001). Among 330 asymptomatic patients at baseline, galectin-3 was neither predictive of outcome in univariate analysis (p = 0.73), nor after adjustment for age, gender, rhythm, creatinine clearance and AS severity (p = 0.66). The authors concluded that in a prospective cohort of patients with a wide range of AS severity, galectin-3 was not associated with AS severity or functional status. Main determinants of galectin-3 were age, hypertension and renal function. They stated that galectin-3 did not provide prognostic information on the occurrence of AS-related events; and that these findings did not support the use of galectin-3 in the decision-making process of asymptomatic patients with AS.

Galectin-3 Test for the Prediction of Outcome in Individuals with Stable Dilated Cardiomyopathy
Wojciechowska and colleagues (2017) noted that dilated cardiomyopathy (DCM) is the 3rd cause of HF and the most frequent cause of heart transplantation (HT). The value of biomarkers in prognostic stratification may be important in identifying patients for more advanced treatment. Assessment of serum galectin-3 (Gal-3) and ST2 as biomarkers of unfavorable outcome (death and combined end-point: HT or death or left ventricular assist device [LVAD] implantation) in stable DCM patients. A total of 107 DCM patients aged 39 to 56 years were included into the study and followed-up for a mean of 4.8 years; Gal-3 and ST2 concentrations were measured using ELISA tests. Clinical data, treatment, laboratory parameters, NT-proBNP, Gal-3 and ST2 measured at time of inclusion were assessed as risk factors for reaching the study end-points using log rank test and Cox proportional-hazards model. During follow-up, 27 patients died, 40 achieved combined end-point; ROC curves indicated cut-off value of ST2 -- 17.53 ng/ml, AUC-0.65(0.53 to 0.76) and of NT-proBNP -- 669 pg/ml, AUC 0.61(0.50 to 0.73) for prediction of death. In multi-variate analysis, ST2 was predictor of death (HR per unit increase in log ST2 2.705, 95 % CI: 1.324 to 5.528, p = 0.006) and combined end-point (HR per unit increase in log ST2 2.753, 95 % CI: 1.542 to 4.914, p < 0.001). The authors concluded that NT-proBNP was predictive variable only for death in multi-variate analysis; Gal-3 concentration was not associated with adverse outcome; ST2 but not Gal-3 may be useful for predicting adverse outcome in stable DCM patients.

Appendix

The NYHA classification of HF is a 4-tier system that categorizes patients based on subjective impression of the degree of functional compromise. The 4 NYHA functional classes are as follows:
Class I:

Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain. Symptoms only occur on severe exertion.

Class II:

Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity (e.g., moderate physical exertion such as carrying shopping bags up several flights or stairs) results in fatigue, palpitation, dyspnea, or anginal pain.

Class III:

Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity (i.e., mild exertion) causes fatigue, palpitation, dyspnea, or anginal pain.

Class IV:

Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of cardiac insufficiency or of the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.
### CPT Codes / HCPCS Codes / ICD-10 Codes

Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+".

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
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</thead>
<tbody>
<tr>
<td></td>
<td><strong>Biventricular Pacing:</strong></td>
</tr>
<tr>
<td></td>
<td><strong>CPT codes covered if selection criteria are met:</strong></td>
</tr>
<tr>
<td>33208</td>
<td>Insertion or replacement of permanent pacemaker with transvenous electrode(s); atrial and ventricular</td>
</tr>
<tr>
<td>33213</td>
<td>Insertion of pacemaker pulse generator only; with existing dual leads</td>
</tr>
<tr>
<td>33214</td>
<td>Upgrade of implanted pacemaker system, conversion of single chamber system to dual chamber system (includes removal of previously placed pulse generator, testing of existing lead, insertion of new lead, insertion of new pulse generator)</td>
</tr>
<tr>
<td>33224</td>
<td>Insertion of pacing electrode, cardiac venous system, for left ventricular pacing, with attachment to previously placed pacemaker or pacing cardioverter-defibrillator pulse generator (including revision of pocket, removal, insertion and/or replacement of existing generator)</td>
</tr>
<tr>
<td>33225</td>
<td>Insertion of pacing electrode, cardiac venous system, for left ventricular pacing, at time of insertion of pacing cardioverter-defibrillator or pacemaker pulse generator (eg, for upgrade to dual chamber system) (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td></td>
<td><strong>CPT codes not covered for indications listed in the CPB:</strong></td>
</tr>
<tr>
<td>0515T</td>
<td>Wireless cardiac stimulation system for left ventricular pacing</td>
</tr>
<tr>
<td>0522T</td>
<td>Wireless cardiac stimulation system for left ventricular pacing</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>--------</td>
<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>82777</td>
<td>Galectin-3</td>
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Other CPT codes related to the CPB:

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<th>Code</th>
<th>Code Description</th>
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<tr>
<td>83520</td>
<td>Immunoassay for analyte other than infectious agent antibody or infectious agent antigen; quantitative, not otherwise specified [galectin-3 test]</td>
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HCPCS codes covered if selection criteria are met:

<table>
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<tr>
<th>Code</th>
<th>Code Description</th>
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<tbody>
<tr>
<td>C1779</td>
<td>Lead, pacemaker, transvenous VDD single pass</td>
</tr>
<tr>
<td>C1785</td>
<td>Pacemaker, dual chamber, rate-responsive (implantable)</td>
</tr>
<tr>
<td>C1882</td>
<td>Cardioverter-defibrillator, other than single or dual chamber (implantable)</td>
</tr>
<tr>
<td>C1898</td>
<td>Lead, pacemaker, other than transvenous VDD single pass</td>
</tr>
<tr>
<td>C1900</td>
<td>Lead, left ventricular coronary venous system</td>
</tr>
<tr>
<td>C2619</td>
<td>Pacemaker, dual chamber, non rate-responsive (implantable)</td>
</tr>
<tr>
<td>C2620</td>
<td>Pacemaker, single chamber, non rate-responsive (implantable)</td>
</tr>
<tr>
<td>C2621</td>
<td>Pacemaker, other than single or dual chamber (implantable)</td>
</tr>
<tr>
<td>G0448</td>
<td>Insertion or replacement of a permanent pacing cardioverter-defibrillator system with transvenous lead(s), single or dual chamber with insertion of pacing electrode, cardiac venous system, for left ventricular pacing</td>
</tr>
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ICD-10 codes covered if selection criteria are met:
<table>
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<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I50.1 - I50.9</td>
<td>Heart failure [members with CHF who are in sinus rhythm and criteria (A or B) are met]</td>
</tr>
</tbody>
</table>

ICD-10 codes not covered for indications listed in the CPB:

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I35.0</td>
<td>Nonrheumatic aortic (valve) stenosis [not covered for prognosis of aortic valve stenosis]</td>
</tr>
<tr>
<td>I42.0</td>
<td>Dilated cardiomyopathy [not covered for Galectin-3]</td>
</tr>
<tr>
<td>I48.0</td>
<td>Atrial fibrillation</td>
</tr>
</tbody>
</table>

Combination Resynchronization-Defibrillation Devices:

CPT codes covered if selection criteria are met:

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<th>Code</th>
<th>Code Description</th>
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</thead>
<tbody>
<tr>
<td>33224</td>
<td>Insertion of pacing electrode, cardiac venous system, for left ventricular pacing, with attachment to previously placed pacemaker or pacing cardioverter-defibrillator pulse generator (including revision of pocket, removal, insertion and/or replacement of generator)</td>
</tr>
<tr>
<td>33225</td>
<td>Insertion of pacing electrode, cardiac venous system, for left ventricular pacing, at time of insertion of pacing cardioverter-defibrillator or pacemaker pulse generator (eg, for upgrade to dual chamber system) (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>33230</td>
<td>Insertion of pacing cardioverter-defibrillator pulse generator only; with existing dual leads</td>
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<tr>
<td>33231</td>
<td>with existing multiple leads</td>
</tr>
<tr>
<td>33240</td>
<td>Insertion of pacing cardioverter-defibrillator pulse generator only; with existing single lead</td>
</tr>
<tr>
<td>33249</td>
<td>Insertion or replacement of permanent pacing cardioverter-defibrillator system with transvenous lead(s), single or dual chamber</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>--------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>33262</td>
<td>Removal of pacing cardioverter-defibrillator pulse generator with replacement of pacing cardioverter-defibrillator pulse generator; single lead system</td>
</tr>
<tr>
<td>33263</td>
<td>with existing dual lead system</td>
</tr>
<tr>
<td>33264</td>
<td>with existing multiple lead system</td>
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</tbody>
</table>

**HCPCS codes covered if selection criteria are met:**

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<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
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</thead>
<tbody>
<tr>
<td>C1779</td>
<td>Lead, pacemaker, transvenous VDD single pass</td>
</tr>
<tr>
<td>C1785</td>
<td>Pacemaker, dual chamber, rate-responsive (implantable)</td>
</tr>
<tr>
<td>C1895</td>
<td>Lead, cardioverter-defibrillator, endocardial dual coil (implantable)</td>
</tr>
<tr>
<td>C1896</td>
<td>Lead, cardioverter-defibrillator, other than endocardial single or dual coil (implantable)</td>
</tr>
<tr>
<td>C1898</td>
<td>Lead, pacemaker, other than transvenous VDD single pass</td>
</tr>
<tr>
<td>C1899</td>
<td>Lead, left pacemaker/cardioverter-defibrillator combination (implantable)</td>
</tr>
<tr>
<td>C1900</td>
<td>Lead, left ventricular coronary venous system</td>
</tr>
<tr>
<td>C2619</td>
<td>Pacemaker, dual chamber, non rate-responsive (implantable)</td>
</tr>
<tr>
<td>C2620</td>
<td>Pacemaker, single chamber, non rate-responsive (implantable)</td>
</tr>
<tr>
<td>C2621</td>
<td>Pacemaker, other than single or dual chamber (implantable)</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>------</td>
<td>------------------</td>
</tr>
<tr>
<td>G0448</td>
<td>Insertion or replacement of a permanent pacing cardioverter-defibrillator system with transvenous lead(s), single or dual chamber with insertion of pacing electrode, cardiac venous system, for left ventricular pacing</td>
</tr>
</tbody>
</table>

**ICD-10 codes covered if selection criteria are met [members who are at high risk for sudden cardiac death]:**

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<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I20.0</td>
<td>Acute, subacute, and old myocardial infarction [prior heart attack and episode of non-sustained VT, with an inducible ventricular tachyarrhythmia]</td>
</tr>
<tr>
<td>I22.9</td>
<td></td>
</tr>
<tr>
<td>I24.0</td>
<td></td>
</tr>
<tr>
<td>I25.2</td>
<td></td>
</tr>
<tr>
<td>I46.2</td>
<td>Cardiac arrest due to underlying cardiac condition [ventricular tachyarrhythmias or LVEF less than or equal to 30%]</td>
</tr>
<tr>
<td>I47.1</td>
<td>Supraventricular tachycardia [with at least 1 episode of cardiac arrest]</td>
</tr>
<tr>
<td>I47.2</td>
<td>Ventricular tachycardia [with at least 1 episode of cardiac arrest or recurrent tachycardia]</td>
</tr>
<tr>
<td>I48.0</td>
<td>Atrial fibrillation</td>
</tr>
<tr>
<td>Z86.74</td>
<td>Personal history of sudden cardiac arrest [as a result of ventricular tachyarrhythmias or LVEF less than or equal to 30%]</td>
</tr>
</tbody>
</table>

**Cardiac resynchronization therapy with wireless left ventricular endocardial pacing - no specific code:**

**ICD-10 codes not covered for indications listed in the CPB:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
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<tbody>
<tr>
<td>I50.1</td>
<td>Heart failure</td>
</tr>
<tr>
<td>I50.9</td>
<td></td>
</tr>
</tbody>
</table>

The above policy is based on the following
references:


Proprietary


46. Bradley DJ, Shen WK. Atrioventricular junction ablation combined with either right ventricular pacing or cardiac resynchronization therapy for atrial fibrillation: The need for large-scale randomized trials. Heart Rhythm. 2007;4(2):224-232.


48. Vardas PE, Auricchio A, Blanc JJ, et al; European Society of Cardiology; European Heart Rhythm Association. Guidelines for cardiac pacing and cardiac resynchronization therapy: The task force for cardiac
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progression by cardiac resynchronization therapy in patients with asymptomatic or mildly symptomatic left ventricular dysfunction: Insights from the European cohort of the REVERSE (Resynchronization Reverses Remodeling in Systolic Left Ventricular Dysfunction) trial. J Am Coll Cardiol. 2009;54(20):1837-1846.


61. BlueCross BlueShield Association (BCBSA), Technology Evaluation Center (TEC). Cardiac resynchronization therapy for mild congestive heart failure. TEC Assessment Program. Chicago, IL: BCBSA; April, 2010;24(8).


72. BlueCross BlueShield Association (BCBSA), Technology Evaluation Center (TEC). Cardiac resynchronization therapy for mild heart failure. TEC Assessment Program. Chicago, IL: BCBSA; July 2011;26(1).


89. Friedman DJ, Singh JP, Curtis JP, et al. Comparative effectiveness of CRT-D versus defibrillator alone in HF


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Amendment to
Aetna Clinical Policy Bulletin Number: 0610 Biventricular Pacing (Cardiac Resynchronization Therapy)/Combination Resynchronization-Defibrillation Devices for Congestive Heart Failure

There are no amendments for Medicaid.