Clinical Policy Bulletin:
Nesiritide (Natrecor)

Number: 0709

Policy

I. Aetna considers nesiritide (Natrecor) medically necessary for the acute management of members with acutely decompensated congestive heart failure (CHF) who have dyspnea at rest or with minimal activity.

II. Aetna considers peri-operative nesiritide administration in members with left ventricular dysfunction undergoing cardiac surgery experimental and investigational because its effectiveness for this indication has not been established.

III. Aetna considers intermittent infusion of nesiritide in persons who are not acutely decompensated or scheduled repetitive use experimental and investigational, as is use of nesiritide to enhance diuresis, to improve renal function, prophylactic use of nesiritide for the prevention of acute kidney injury, adjuvant use following cardiac surgery, and all other indications because its effectiveness for these indications has not been established.

IV. Aetna considers subcutaneous administration of B-type natriuretic peptide experimental and investigational for the treatment of heart failure because the effectiveness of this approach has not been established.

See also CPB 0618 - Brain Natriuretic Peptide Testing.

Background

Heart failure is the leading cause of hospitalizations in the United States and is associated with significant morbidity, mortality and resource utilization. Established treatments for congestive heart failure (CHF) have been shown to improve outcomes, but treatment for decompensated HF remains largely empiric.

Brain natriuretic peptide, also known as B-type natriuretic peptide (BNP), is a neurohormone that is secreted by the left ventricle in response to an increase in
tension (both pressure and volume load) in the ventricular wall. The physiological actions of BNP include natriuresis, vasodilation and neurohormonal modulation. Brain natriuretic peptide has emerged as a neurohormone with multiple roles in the management of HF. The BNP assay is currently used in the urgent care setting to distinguish dyspnea due to HF from pulmonary disease. In general, BNP levels of under 100 pg/ml exclude acutely decompensated CHF, while levels over 500 pg/ml indicate decompensation.

Nesiritide is a recombinant form of endogenous human BNP. It has been shown to decrease cardiac filling pressures, increase cardiac index and improve the clinical status of patients with acute decompensated HF. In August 2001, nesiritide (Natrecor) was approved by the U.S. Food and Drug Administration (FDA) for the treatment of acutely decompensated CHF who have dyspnea at rest or with minimal activity. The recommended dosing regimen for nesiritide is an intravenous bolus of 2 µg/kg body weight followed by a continuous infusion of 0.01 µg/kg/min over an extended period of time, from a few hours up to, but no longer than, 48 hours.

Patients with chronic decompensated HF may have inadequate hemodynamic responses or limited tolerance of oral heart failure medications and therefore may require parenteral administration of vasoactive agents. Elkayam et al (2004) reported an advantage of nesiritide compared with high-dose nitroglycerin in the treatment of patients with decompensated HF. Nesiritide resulted in an early (15 minutes or less) decrease in pulmonary capillary wedge pressure, which was sustained throughout the 24-hour study period without the need for up-titration. By contrast, the onset of the nitroglycerin-mediated hemodynamic effect was delayed, and despite aggressive up-titration, the decrease in pulmonary capillary wedge pressure was gradually attenuated because of the early development of tolerance. Aronson and Burger (2004) evaluated the effects of nesiritide compared with dobutamine on time-domain indices of heart rate variability (HRV) in patients with decompensated CHF (n = 185). These investigators concluded that low-dose nesiritide therapy in patients with decompensated CHF improves indices of overall HRV and parasympathetic modulation, particularly if HRV is severely depressed at baseline. Moreover, dobutamine and possibly high-dose nesiritide can potentially lead to further deterioration of autonomic dysregulation.

Natrecor has also been used for so-called “tune-up” of the heart in outpatient clinics, where patients with HF receive regular infusions, sometimes weekly or more often, over several months. Typically, it is infused over 6 to 8 hours once-weekly. While the drug can almost instantly improve shortness of breath and pressure on the heart, its long-term benefit is unclear. Yancy et al (2004) discussed the potential role of nesiritide as an outpatient treatment option for patients with symptomatic HF who were at high-risk for repeated admissions, a syndrome now described as “chronic decompensated heart failure”. The authors stated that the use of outpatient intravenous nesiritide is a promising therapeutic option for symptomatic chronic decompensated HF patients. The authors noted, however, that additional studies are needed to ascertain the effect of outpatient infusions of nesiritide on rates of morbidity and mortality in advanced HF.

In 2 meta-analyses, Sackner-Bernstein et al (2005a and 2005b) examined the safety of nesiritide relative to noninotrope-based control therapies, primarily
consisting of diuretics or vasodilators. These researchers reported that compared with noninotrope-based control therapy, nesiritide may be associated with a worsening of renal function as well as an increased risk of death after treatment for acutely decompensated HF and concluded that the possibility of an increased risk of death should be investigated in a large-scale, adequately powered, randomized, controlled trial before routine use of nesiritide for acutely decompensated HF. These findings resulted in a revision in the FDA-approved prescribing information for Natrecor to indicate an increased risk of fatal renal problems in patients treated with the drug. The “Adverse Reactions/Effect on Mortality” section of the prescribing information has been revised to include information on published reports that suggest that Natrecor may have adverse effects on survival and kidney function compared to control agents (generally nitroglycerin and diuretics) - 5.3% of patients treated with Natrecor died, compared with 4.3% in control groups. However, the revised prescribing information notes that because of the small numbers of patients involved these differences did not reach statistical significance (FDA, 2005).

An expert panel of cardiology and HF clinicians convened in June 2005 at the request of the manufacturer to evaluate data associated with the treatment of acute HF by means of Natrecor. The panel provided the following 3 recommendations on the use of nesiritide (Braunwald et al, 2005):

I. The use of nesiritide should be strictly limited to patients presenting to the hospital with acutely decompensated CHF who have dyspnea at rest, as were the patients in the largest trial that led to approval of the drug. Physicians considering the use of nesiritide should consider its efficacy in reducing dyspnea, the possible risks of the drug, and the availability of alternate therapies to relieve the symptoms of CHF.

II. Nesiritide should not be used to replace diuretics. Furthermore, because sufficient evidence is not currently available to demonstrate benefit for the applications listed below, nesiritide should not be used for:

   A. Enhancement of diuresis
   B. Improvement of renal function
   C. Intermittent outpatient infusion
   D. Scheduled repetitive use

III. The manufacturer should immediately undertake a pro-active educational program to inform physicians regarding the conditions and circumstances in which nesiritide should and should not be used. Sponsor supported communications, including review articles of nesiritide, should reflect the above recommendations. Scios, Inc. should ensure that current and future marketing and sales activities related to nesiritide are consistent with this educational program.

In an editorial published in the New England Journal of Medicine, Topol (2005) stated that the European Agency for the Evaluation of Medicinal Products has not approved nesiritide and is waiting for the results of a trial involving 1,900 patients. The author stated that nesiritide has not yet met the minimal criteria for safety and effectiveness. Topol explained that, until a trial definitively proves that this drug reduces the risk of death or repeated hospitalization for heart failure, there will be
questions about the appropriateness of the drug’s use or even commercial availability.

The Centers for Medicare & Medicaid Services (CMS) has determined that “there is sufficient evidence to conclude that the use of Nesiritide for the treatment of chronic heart failure is not reasonable and necessary for Medicare beneficiaries in any setting.”

According to the FDA-approved product labeling, nesiritide is contraindicated in persons who are hypersensitive to any of its components. The labeling states that it should not be used as primary therapy for individuals with cardiogenic shock or in persons with a systolic blood pressure less than 90 mm Hg.

Additional studies published since the CMS determination have found nesiritide ineffective in chronic HF. Yancey et al (ACC, 2007) presented the results of the FUSION II trial (Follow-Up Serial Infusions of Nesiritide in Advanced Heart Failure), where more than 900 patients with end-stage chronic HF were randomized to receive nesiritide or placebo infusions once- or twice-weekly for 12 weeks. Rates of death or subsequent hospitalizations for heart or kidney problems did not differ significantly between the 2 groups.

Studies are examining the potential for peri-operative use of nesiritide in persons with reduced left ventricular dysfunction undergoing cardiac surgery. In a prospective, open-label, randomized controlled trial, Brackbill et al (2007) examined if peri-operative infusion of nesiritide improves clinical outcomes compared with milrinone therapy. A total of 40 consecutive hemodynamically stable patients with ejection fractions 35 % or less undergoing coronary artery bypass grafting (CABG) surgery were included in this study. Patients were randomized to receive either an intra-operative bolus of nesiritide or milrinone followed by a 24-hour infusion of each agent. Length of post-operative intensive care unit stay was the primary outcome variable evaluated. Incidence of post-operative HF, 30-day re-admission rates, mortality, and other clinical parameters were also compared. Patients receiving nesiritide had a mean +/- SD post-operative intensive care unit stay of 50.6 +/- 46.8 hours compared with 44.1 +/- 23.5 hours in those receiving milrinone (p = 0.578). Incidence of post-operative HF was also not significantly different between the drugs (p = 0.259). Thirty-day follow-up confirmed no difference in hospital re-admission rates between nesiritide and milrinone (p = 0.661). No differences in mortality were observed during hospitalization or 30 days of follow-up. The authors concluded that nesiritide does not decrease post-operative intensive care unit stay or other clinical parameters compared with milrinone in high-risk patients with hemodynamically stable left-ventricular function undergoing CABG surgery.

In a prospective, double-blinded study (the NAPA Trial), Mentzer and colleagues (2007) ascertained the role nesiritide might play in patients with left ventricular dysfunction undergoing CABG using cardiopulmonary bypass (CPB). Patients with ejection fraction less than or equal to 40 % who were undergoing CABG with anticipated use of CPB were randomly assigned to receive either nesiritide or placebo, in addition to usual care, for 24 to 96 hours after induction of anesthesia. Post-operative renal function, hemodynamics, and drug use (primary end points) were assessed in patients who underwent CABG using CPB; mortality and safety (secondary end points) were assessed in all patients who received the study drug.
Of 303 randomized patients, 279 received the study drug and 272 underwent CABG using CPB. Compared with placebo, nesiritide was associated with a significantly attenuated peak increase in serum creatinine (0.15 +/- 0.29 mg/dl versus 0.34 +/- 0.48 mg/dl; p < 0.001) and a smaller fall in glomerular filtration rate (-10.8 +/- 19.3 ml/min/1.73 m(2) versus -17.2 +/- 21.9 ml/min/1.73 m(2); p = 0.001) during hospital stay or by study day 14, and a greater urine output (2,926 +/- 1,179 ml versus 2,350 +/- 1,066 ml; p < 0.001) during the initial 24 hours after surgery.

In addition, nesiritide-treated patients had a shorter hospital stay (p = 0.043) and lower 180-day mortality (p = 0.046). The authors concluded that nesiritide in the setting of CABG with CPB is associated with improved post-operative renal function and possibly enhanced survival.

In an editorial that accompanied the afore-mentioned article, Belenkie (2007) stated that "there is still much to learn regarding how to use this promising agent. The NAPA trial provides encouraging results in one subgroup of patients who might benefit from the use of nesiritide, but more comprehensive data are required before promoting routine use in this population".

Yancy and colleagues (2008) reported the findings of the the second Follow-Up Serial Infusions of Nesiritide (FUSION II) trial, which was a randomized, double-blind, placebo-controlled study of outpatient serial nesiritide infusions for patients with American College of Cardiology/American Heart Association stage (ACC/AHA) C/D heart failure. Patients with 2 recent HF hospitalizations, ejection fraction less than 40 %, and New York Heart Association (NYHA) class IV symptoms, or NYHA class III symptoms with creatinine clearance less than 60 ml/min, were randomized to nesiritide (2 µg/kg bolus plus 0.01 µg/kg/minute infusion for 4 to 6 hours) or matching placebo, once- or twice-weekly for 12 weeks. All patients were treated to optimal goals with evidence-based medical/device therapy facilitated by careful disease management during the study. The primary end point was time to all-cause death or cardiovascular or renal hospitalization at 12 weeks. A total of 911 patients were randomized and treated. The primary end point occurred in 36.8 % and 36.7 % of the placebo and nesiritide groups, respectively (hazard ratio, 1.03; 95 % confidence interval [CI]: 0.82 to 1.3; log-rank test p = 0.79). There were no statistically significant differences between groups in any of the secondary end points, including the number of cardiovascular or renal hospitalizations, the number of days alive and out of the hospital, change in Kansas City Cardiomyopathy Questionnaire score, or cardiovascular death. Adverse events were similar between groups; nesiritide was associated with more hypotension but less pre-defined worsening renal function. The authors concluded that serial outpatient nesiritide infusions do not provide a demonstrable clinical benefit over intensive outpatient management of patients with advanced ACC/AHA stage C/D heart failure. There is no indication for intermittent outpatient nesiritide infusions in patients with stage C/D heart failure. This is in agreement with the observation of Maeder and co-workers (2008) who noted that despite active research in many additional fields, the use of BNP/N-terminal-proBNP in settings other than management of acute decompensated CHF in the emergency department is not yet based on solid evidence and, thus, seems not to be useful.

In a pilot study, Behera et al (2009) aimed to obtain hemodynamic measurements of nesiritide in children with dilated cardiomyopathy. All subjects younger than 21
years admitted to the pediatric intensive care unit with a diagnosis of dilated cardiomyopathy and submitted to cardiac catheterization were randomized to receive either nesiritide or placebo. Right heart catheterization with Swan-Ganz catheter placement was carried out. Nesiritide was infused over 24 hours. Hemodynamic data were obtained before, during, and after the 24-hour nesiritide infusion. The measures obtained included pulmonary capillary wedge pressure (PCWP), central venous pressure, mean pulmonary arterial pressure (MPAP), systolic blood pressure (SBP), cardiac index, and systemic vascular resistance. The study included 20 children: 9 randomized to nesiritide and 11 to placebo. At 24 hours, the mean decreases in PCWP, MPAP, and SBP were significantly greater for nesiritide than for placebo: PCWP (-5.3 versus 1.2 mm Hg; p = 0.02), MPAP (-8.0 versus 0.4 mm Hg; p = 0.006), SBP (-7.9 versus 2.6 mm Hg; p = 0.04). The authors concluded that nesiritide significantly decreases PCWP, MPAP, and SBP in children with dilated cardiomyopathy. This was a small study that provided hemodynamic measurements in children with dilated cardiomyopathy treated with nesiritide. Further investigation is needed to ascertain the health benefits of this approach in this group of patients.

Randomized controlled trials involving administration of natriuretic peptide in the peri-operative cardiovascular setting have shown inconsistent effects for renal and other clinical endpoints. Nigwekar and Hix (2009) reviewed these trials to ascertain the role of natriuretic peptide administration in the management of cardiovascular surgery-associated renal dysfunction. These investigators concluded that current literature analyzing studies evaluating the administration of natriuretic peptides in cardiovascular surgery may be associated with significant improvements in clinical outcomes. They noted that given the limitations of meta-analysis, these observations need to be confirmed in a larger, adequately powered, prospective multi-center study.

In a prospective, randomized, clinical trial, Ejaz and colleagues (2009) examined if prophylactic use of nesiritide is associated with a reduction in the odds for dialysis or in-hospital mortality in patients undergoing high-risk cardiac surgery. This trial included 94 patients undergoing high-risk cardiac surgery comparing a 5-day course of continuous nesiritide (at a dose of 0.01 microg x kg(-1) x min(-1) started before surgery) versus placebo. The primary end point was dialysis and/or all-cause mortality within 21 days; secondary end points were incidence of acute kidney injury (AKI), renal function, and length of stay. Nesiritide did not reduce the primary end point of incidence of dialysis and/or all-cause mortality through day 21 (6.6 % versus 6.1 %; p = 0.914). Fewer patients receiving nesiritide had AKI (defined as an absolute increase in serum creatinine greater than or equal to 0.3 mg/dL from baseline or a percentage increase in serum creatinine greater than or equal to 50 % from baseline within 48 hours) compared with controls (2.2 % versus 22.4 %; p = 0.004), and mean serum creatinine was lower in the immediate post-operative period in the nesiritide group (1.18 +/- 0.41 mg/dL versus 1.45 +/- 0.74 mg/dL; p = 0.028). However, no difference in length of stay was noted (nesiritide 20.73 +/- 3.05 days versus control 21.26 +/- 4.03 days; p = 0.917). The authors concluded that these findings do not demonstrate a benefit for prophylactic use of nesiritide on the incidence of dialysis and/or death in patients undergoing high-risk cardiac surgery. Although nesiritide may provide some renal protection in the immediate post-operative period, no effect on length of stay was observed.
Lingegowda et al (2010) examined if the observed renal benefits of nesiritide had any long-term impact on cumulative patient survival and renal outcomes. Participants of the Nesiritide Study, a previously reported prospective, double-blind, placebo-controlled, randomized clinical trial investigating the effect of nesiritide on the incidence of dialysis or death at 21 days in adult patients undergoing high-risk cardiovascular surgery, were included in the study. Data of the subjects’ most recent health and renal function status were obtained using institutional review board-approved patient questionnaires, medical records, and the database of the Social Security Administration. Data on all 94 patients from the Nesiritide Study were obtained. The mean follow-up period was 20.8 +/- 10.4 months. No differences in cumulative survival between the groups were noted at follow-up (nesiritide 77.7 % versus placebo 81.6 %, p = 0.798). Patients with in-hospital incidence of AKI had a higher rate of mortality than those with no AKI (AKI 41.4 % versus no AKI 10.7 %, p = 0.002). However, differences in survival time were not significant between the groups when the analysis was restricted to patients with AKI (nesiritide 16.8 +/- 4 months versus placebo 18.5 +/- 2.3 months, p = 0.729). The authors concluded that renal protection provided by nesiritide in the immediate post-operative period was not associated with improved long-term survival in patients undergoing high-risk cardiovascular surgery.

Mitaka et al (2011) evaluated the cardiovascular and renal effects of an atrial natriuretic peptide (ANP, carperitide) and a BNP (nesiritide) for preventing and treating AKI in cardiovascular surgery patients. Electronic databases, including PubMed, EMBASE and references from identified articles were used for a literature search. Data on the infusion of ANP or BNP in cardiovascular surgery patients was collected from 15 randomized controlled trials (RCTs) and combined. The infusion of ANP or BNP increased the urine output and creatinine clearance or glomerular filtration rate, and reduced the use of diuretics and the serum creatinine levels. A meta-analysis showed that ANP infusion significantly decreased peak serum creatinine levels, incidence of arrhythmia and renal replacement therapy. The meta-analysis also showed that ANP or BNP infusion significantly decreased the length of intensive-care unit stay and hospital stay compared with controls. However, the combined data were insufficient to determine how ANP or BNP infusion during the peri-operative period influences long-term outcome in cardiovascular surgery patients. The authors concluded that the infusion of ANP or BNP may preserve post-operative renal function in cardiovascular surgery patients. Moreover, they stated that a large, multi-center, prospective RCT is needed to evaluate the therapeutic potential of ANP or BNP in preventing and treating AKI in the cardiovascular surgical setting.

O’Connor et al (2011) stated that nesiritide is approved in the United States for early relief of dyspnea in patients with acute HF. Previous meta-analyses have raised questions regarding renal toxicity and the mortality associated with this agent. These investigators randomly assigned 7,141 patients who were hospitalized with acute HF to receive either nesiritide or placebo for 24 to 168 hours in addition to standard care. Co-primary end points were the change in dyspnea at 6 and 24 hours, as measured on a 7-point Likert scale, and the composite end point of re-hospitalization for HF or death within 30 days. Patients randomly assigned to nesiritide, as compared with those assigned to placebo, more frequently reported markedly or moderately improved dyspnea at 6 hours.
(44.5 % versus 42.1 %, p = 0.03) and 24 hours (68.2 % versus 66.1 %, p = 0.007), but the pre-specified level for significance (p ≤ 0.005 for both assessments or p ≤ 0.0025 for either) was not met. The rate of re-hospitalization for HF or death from any cause within 30 days was 9.4 % in the nesiritide group versus 10.1 % in the placebo group (absolute difference, -0.7 percentage points; 95 % CI: -2.1 to 0.7; p = 0.31). There were no significant differences in rates of death from any cause at 30 days (3.6 % with nesiritide versus 4.0 % with placebo; absolute difference, -0.4 percentage points; 95 % CI: -1.3 to 0.5) or rates of worsening renal function, defined by more than a 25 % decrease in the estimated glomerular filtration rate (31.4 % versus 29.5 %; odds ratio, 1.09; 95 % CI: 0.98 to 1.21; p = 0.11). The authors concluded that nesiritide was not associated with an increase or a decrease in the rate of death and re-hospitalization and had a small, non-significant effect on dyspnea when used in combination with other therapies. It was not associated with a worsening of renal function, but it was associated with an increase in rates of hypotension. They stated that on the basis of these results, nesiritide cannot be recommended for routine use in the broad population of patients with acute HF.

The Institute for Clinical Systems Improvement's clinical practice guideline on "Heart failure in adults" (ICSI, 2011) recommended that nesiritide be reserved for patients with acutely decompensated HF who remain volume over-loaded despite aggressive treatment with diuretics/vasodilators, display tolerance and/or resistance to vasodilators or diuretics, or demonstrate significant side-effects to other vasodilators.

Until further studies are done, it is the opinion of this work group that vasodilators and/or diuretics other than nesiritide be attempted prior to trialing nesiritide. Nesiritide, when effective, improves dyspnea but has not reduced length of hospitalization or improved mortality. Nesiritide may remain an option with subspecialty consultation, but standard use is not currently supported by evidence. Nesiritide is FDA-approved for the intravenous treatment of patients with acutely decompensated HF who have dyspnea at rest or with minimal activity.

In patients hospitalized with decompensated HF, nesiritide was shown to have a modest reduction in hemodynamic function and clinical status [Quality of evidence: Moderate].

The ASCEND-HF trial showed that nesiritide was indeed safe to use as it was not associated with any change in mortality or renal function as compared to standard care [Quality of evidence: Moderate]. The benefit, however, was a modest improvement in symptoms (shortness of breath) and did not even reach statistical significance. Thus, it is yet to be defined as to which subset, if any, of patients with acute decompensated heart failure (ADHF) could benefit from nesiritide.

If nesiritide is used, take into consideration the following:

The best candidates for nesiritide therapy are patients with decompensated HF who have clinical evidence of fluid over-load and/or raised central venous pressure [Quality of evidence: Low]. There is little experience with infusions of nesiritide for more than 48 hours.
Nesiritide is not routinely recommended even when patients do not positively respond to nitroglycerin infusion and should be used in consultation with cardiology because of its minimal benefit.

In a randomized double-blind placebo-controlled proof of concept study, Chen et al (2012) examined safety and effectiveness of 8 weeks of chronic subcutaneous (SC) BNP administration in human Stage-C HF. This study compared 8 weeks of SC BNP (10 μg/kg of body weight, bid) (n = 20) with placebo (n = 20) in patients with ejection fraction < 35 % and NYHA functional class II to III HF. Primary outcomes were left ventricular (LV) volumes and LV mass determined by cardiac magnetic resonance imaging. Secondary outcomes include LV filling pressure by Doppler echo, humor function, and renal function. Eight weeks of chronic SC BNP resulted in a greater reduction of LV systolic and diastolic volume index and LV mass index as compared with placebo. There was a significantly greater improvement of Minnesota Living with Heart Failure score, LV filling pressure as demonstrated by the reductions of E/e’ ratio, and decrease in left atrial volume index as compared with placebo. Glomerular filtration rate was preserved with SC BNP, as was the ability to activate plasma 3',5'-cyclic guanosine monophosphate (p < 0.05 versus placebo). The authors concluded that in this pilot proof of concept study, chronic protein therapy with SC BNP improved LV remodeling, LV filling pressure, and Minnesota Living with Heart Failure score in patients with stable systolic HF on optimal therapy. Renin-angiotensin was suppressed, and glomerular filtration rate was preserved. Subcutaneous BNP represents a novel, safe, and effective protein therapeutic strategy in human HF. Moreover, they stated that further studies are needed to determine whether these physiologic observations can be translated into improved clinical outcomes and ultimately delay the progression of HF.

In an editorial that accompanied the afore-mentioned study, Ahmad and Felker (2012) stated that “future trials will be needed to refine dosing and patient selection as well as to provide more definitive evidence for clinical efficacy …. Whether BNP therapy can be successfully reincarnated as an “enlightened” therapy for HF therapy remains to be seen, and further investigation will determine whether SC administration of BNP might represent the “middle way” to successful HF therapy”.

CPT Codes / HCPCS Codes / ICD-9 Codes

HCPCS codes covered if selection criteria are met:

J2325  Injection, nesiritide, 0.1 mg

ICD-9 codes covered if selection criteria are met:

428.21  Systolic heart failure, acute
428.23  Systolic heart failure, acute on chronic
428.31  Diastolic heart failure, acute
428.33  Diastolic heart failure, acute on chronic
428.41  Combined systolic and diastolic heart failure, acute
428.43  Combined systolic and diastolic heart failure, acute on chronic

**ICD-9 codes not covered for indications listed in the CPB:**

580.0 - 593.9  Nephritis, nephrotic syndrome, and nephrosis, and other diseases of kidney and ureter

**Other ICD-9 codes related to the CPB:**

411.1  Intermediate coronary syndrome
415.11 - 415.19  Pulmonary embolism and infarction
427.31  Atrial fibrillation
785.51  Cardiogenic shock
786.00 - 786.09  Symptoms involving respiratory system and other chest symptoms
995.91  Systemic inflammatory response syndrome due to infectious process without organ dysfunction

The above policy is based on the following references:


