Medical Policy

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***Current Policy Effective Date: 11/1/24**
(See policy history boxes for previous effective dates)

Title: Enhanced External Counterpulsation (EECP)

Description/Background

Enhanced external counterpulsation (EECP) is a noninvasive treatment used to augment diastolic pressure; decrease left ventricular afterload, and increase venous return. It has been studied primarily as a treatment for patients with refractory angina and heart failure, as well as for other indications such as ischemic stroke.

Enhanced external counterpulsation (EECP) uses timed, sequential inflation of pressure cuffs on the calves, thighs, and buttocks to augment diastolic pressure, decrease left ventricular afterload, and increase venous return. The proposed mechanism of action is the augmentation of diastolic pressure by displacement of a volume of blood backward into the coronary arteries during diastole when the heart is in a state of relaxation and resistance in the coronary arteries is at a minimum. The resulting increase in coronary artery perfusion pressure may enhance coronary collateral development or increase flow through existing collaterals. In addition, when the left ventricle contracts, it faces a reduced aortic pressure to work against, since the counterpulsation has somewhat emptied the aorta. EECP has been primarily investigated as a treatment for chronic stable angina.

Intra-aortic balloon counterpulsation is a more familiar, invasive form of counterpulsation that is used as a method of temporary circulatory assistance for the ischemic heart, often after an acute myocardial infarction (MI). In contrast, EECP is thought to provide a permanent effect on the heart by enhancing the development of coronary collateral development. A full course of therapy usually consists of 35 one-hour treatments, which may be offered once or twice daily, usually 5 days per week. The multiple components of the procedure include the use of the device itself, finger plethysmography to follow the blood flow, continuous electrocardiograms (EKGs) to

trigger inflation and deflation, and optional use of pulse oximetry to measure oxygen saturation before and after treatment.

Regulatory Status

A variety of enhanced external counterpulsation (EECP) devices have been cleared for marketing by the Food and Drug Administration (FDA) through the 510(k) process. Examples of EECP devices with FDA clearance are outlined in Table 1.

Table 1: FDA-Cleared EECP Devices

Device	Manufacturer	Clearance Date	Indications
External Counterpulsation System	Vamed Medical Instrument	Sep 2019	• Chronic stable angina refractory to optimal anti-anginal medical therapy and without options for revascularization • In healthy patients to improve vasocilation, increase Vo2, and increase blood flow
Pure Flow External Counter-Pulsation Device	Xtreem Pulse	May 2018	• Chronic stable angina refractory to optimal anti-anginal medical therapy and without options for revascularization • In healthy patients to improve vasodilation, increase Vo2, and increase blood flow
Renew® NCP-5 External Counterpulsation System	Renew Group (Rockville MD)	Dec 2015	• Treatment of chronic stable angina refractory to optimal anti-anginal medical therapy and without options for revascularization • In healthy patients to improve vasodilation increase Vo_2, and increase blood flow
CardiAssist™ Counterpulsation System	Cardiomedics (Irvine, CA)	Mar 2005	• Treatment of ischemic heart disease by increasing perfusion during diastole in people with chronic angina pectoris, congestive heart failure, myocardial infarction, and Cardiogenic shock
ACS Model NCP-2 External Counterpulsation Device	Applied Cardiac Systems (Laguna Hills, CA)	Aug 2004	• Stable or unstable angina pectoris • Acute myocardial infarction • Cardiogenic shock • Congestive heart failure
EECP® Therapy System	Vasomedical (Westbury, NY)	Mar 2004	• Stable or unstable angina pectoris • Acute myocardial infarction • Cardiogenic shock • Congestive heart failure

EECP: enhanced external counterpulsation; FDA: Food and Drug Administration; Vo_2: oxygen consumption

FDA product code: DRN

Medical Policy Statement

- The safety and effectiveness of enhanced external counterpulsation (EECP) in the treatment of chronic stable angina have been established. It may be

considered as an alternative treatment for chronic stable angina in those patients who are refractory to maximal medical management and who are not suitable for invasive treatment techniques.

- The use of EECP in patients with a diagnosis of any medical condition other than stable, chronic angina is experimental/investigational. EECP has not been scientifically demonstrated to improve patient clinical outcomes for other conditions, such as erectile dysfunction, heart failure, ischemic stroke or unstable angina.

Inclusionary and Exclusionary Guidelines

Inclusions:
EECP treatment should be limited to one or two times per day with a maximum of 35 one-hour treatments. Maximum treatment hours do not have to be consecutive.

Patients selected for EECP for the treatment of chronic stable angina should meet the following criteria:

- Angina levels II, III or IV (Canadian Cardiovascular Society Classification) for patients not readily amenable to surgical intervention
- Documented evidence of coronary artery disease (CAD) evidenced by one of the following criteria:
  - > 70% stenosis of at least one or more major coronary arteries, proven angiographically
  - History of myocardial infarct (MI) documented by ECG (presence of Q wave) and elevation of cardiac enzymes
  - Positive (for MI or ischemia) nuclear exercise stress test
  - Positive exercise treadmill test (ETT)

Relative contraindications:

- Atrial fibrillation or frequent PVC's that interfere with EECP triggering
- Baseline electrocardiogram (ECG) abnormalities that will interfere with the interpretation of the exercise ECG
- Blood pressure > 180/110 mm Hg
- Cardiac catheterization in the preceding two weeks
- History of varicosities, deep vein thrombosis, phlebitis or stasis ulcer, bleeding diathesis, warfarin use
- Left ventricular ejection fraction <30%
- Myocardial Infarction or coronary artery bypass in the preceding three months
- Non-bypassed left main artery stenosis > 50%
- Overt congestive heart failure
- Patients unable to undergo treadmill testing or who are in a cardiac rehabilitation program
- Permanent pacemaker or implantable defibrillator
- Severe symptomatic peripheral vascular disease
- Significant valvular heart disease
- Unstable angina
- Women with childbearing potential or who are pregnant

Exclusions:

- All other conditions not listed above including erectile dysfunction, heart failure, ischemic stroke or unstable angina.

CPT/HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure.)*

Established codes:

G0166

Other codes (investigational, not medically necessary, etc.):

N/A

Rationale

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function-including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Promotion of greater diversity and inclusion in clinical research of historically marginalized groups (e.g., People of Color [African-American, Asian, Black, Latino and Native American]; LGBTQIA (Lesbian, Gay, Bisexual, Transgender, Queer, Intersex, Asexual); Women; and People with Disabilities [Physical and Invisible]) allows policy populations to be more reflective of and findings more applicable to our diverse members. While we also strive to use inclusive language related to these groups in our policies, use of gender-specific nouns (e.g., women, men, sisters, etc.)

will continue when reflective of language used in publications describing study populations.

CHRONIC STABLE ANGINA

Clinical Context and Therapy Purpose

The purpose of enhanced external counterpulsation (EECP) is to provide a treatment option that is an alternative to or an improvement on existing therapies, such as guideline-directed medical management, in patients with chronic stable angina, heart failure, or other indications related to ischemia or vascular dysfunction.

The following **PICOs** was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with chronic stable angina, heart failure, or other indications related to ischemia or vascular dysfunction.

Interventions

The therapy being considered is EECP. EECP is a noninvasive treatment used to augment diastolic pressure, decrease left ventricular afterload, and increase venous return.

Comparators

Comparators of interest include guideline-directed medical management.

Outcomes

The general outcomes of interest are overall survival (OS), symptoms, morbid events, and functional outcomes.

Available literature has followed patients for up to 3 years.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs.
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

The literature base consists of a low number of RCTs, some of which have reported relevant clinical outcomes, and others that have reported intermediate or physiologic outcome measures. Also, there are a large number of observational studies, including publications from EECP registries and case series, that have generally reported pretreatment and posttreatment measures of EECP effectiveness.

Review of Evidence

Randomized Controlled Trials

In 1999, Arora et al presented results of the MUST-EECP trial.[1] MUST-EECP applied a randomized, controlled, double-blinded protocol that compared active treatment to placebo (inactive counterpulsation [CP] sham treatment) among 139 patients with Canadian Cardiovascular Society (CCS) Classification Scales (a functional assessment tool based on the level of exertion that elicits symptoms) class I–III chronic, stable angina. Four outcomes were examined:

- Self-reported frequency of angina, analyzed two ways;
- Self-reported use of on-demand nitroglycerin;
- Exercise duration tolerance testing; and
- Time to exercise-induced ischemia (defined as time to depression of ≥1mm in the ST segment on electrocardiogram).

All patients underwent the same 35-hour protocol, followed by an exercise tolerance test within 1 week of completion of therapy. Follow-up beyond the treatment period was not conducted. Intention-to-treat analyses were reported for the angina count and nitroglycerin usage outcomes only. There was a statistically significant difference ($p=0.01$) between groups in the change in time to ≥1 mm ST segment depression. Patients in the EECP group had an average difference of 37 seconds longer time to ST segment depression compared to the sham-treated group. There was no significant difference between treatment groups in the change in exercise duration from baseline to the post-treatment period ($p<0.31$). In addition, there were no statistically significant differences between groups with respect to angina counts ($p<0.09$) or nitroglycerin use ($p>0.1$).

In addition to a number of methodological limitations found in the design, execution, and reporting of this study, the magnitude of the benefit reported is not large. Of the four endpoints of interest, only the time to ST segment depression was statistically different in the EECP group compared to the sham-treated group. The clinical significance of a 37-second improvement in time to ST segment depression is unknown, but given that it occurred while the other three endpoints were statistically unchanged with therapy, does not suggest a marked improvement. That both groups showed increased exercise duration suggests a degree of placebo effect; exercise duration possesses a motivational component that time to ST segment depression does not.

In 2002, Arora et al published a 12-month follow-up study to the MUST-EECP trial.[2] However, only 71 (54%) of the original 139 subjects were included in the study. Subjects treated with EECP reported greater improvement in several quality-of-life scales. However, such findings could not be correlated with treatment response reported in the first study (because of data limitations). The findings are further limited by the small sample size and potentially biased sample of the original subject pool.

A small unblended RCT published by Bondesson et al (2011) addressed a single health outcome (change after 7 weeks in CCS angina class), along with multiple intermediate outcomes.[3] Twenty patients with refractory angina (CCS class III) were randomized to EECP or no EECP. Mean CCS class was significantly improved in the EECP group but not in the no EECP group. At 7-week follow-up, soluble

interleukin-2, receptor measurements significantly increased in the EECP group and significantly decreased in the no EECP group. There were no differences between groups at 7 weeks in resting cutaneous microvascular blood flow or response to acetylcholine, sodium nitroprusside or local heating.

Additional RCTs have reported on intermediate, or physiologic, outcomes. One such RCT (n=20), published by Gloekler et al (2010), compared intracoronary blood flows in patients treated with EECP against those treated with a sham procedure.[4] This trial was designed to detect statistically significant differences in collateral flow rates by angiography, not angina symptoms. After 7 weeks of treatment, collateral flow index increased significantly in the EECP group compared to sham treatment. Similar findings were noted in a comparative study by Buschmann and colleagues of 23 patients published in 2009.[5]

Two publications from a single study reported on blood flow and other measures of arterial function.[6,7] This study randomized 42 patients with coronary artery disease (CAD) and chronic angina to EECP or sham EECP. EECP improved flow-mediated dilation in the brachial and femoral arteries and improved numerous serum markers of blood flow and inflammation. The same study also reported that measures of arterial stiffness were improved in the EECP group. Martin et al randomized 18 patients with abnormal glucose tolerance to EECP or standard care and reported that measures of glucose tolerance, as well as measures of arterial function were improved in the EECP group.

In a 2015 randomized pilot study, Shakouri et al reported on intermediate outcome measures, including plasma nitric oxide, endothelin 1, high-sensitivity C-reactive protein, and QOL, in patients with CAD allocated to 20 sessions of EECP (n=21) or cardiac rehabilitation (n=21).[8] There were no statistically significant improvements in physiologic markers and QOL over time in either group and not statistically significant between-group differences in change in any of the parameters evaluation.

Systematic Reviews

This evidence review was informed by a TEC Assessment (1999) on EECP for chronic stable angina, which was updated in 2002 and again in 2005.[9] These assessments concluded that the evidence was insufficient to determine whether EECP improved the net health outcome or is as beneficial as any established alternatives in patients with chronic stable angina.

Specifically, the 2005 TEC Assessment offered the following observations and conclusions regarding EECP for chronic stable angina[9]:

- The results of the single randomized, controlled trial, the Multicenter Study of Enhanced External Counterpulsation (MUST-EECP), discussed further here, must be interpreted with caution, in view of the high subject dropout rate and uncertainty regarding the clinical significance of the reported improvement in physiologic measures, especially when intent-to-treat analysis is applied.[3, 4]
- Comparative studies of EECP do not address the hard outcomes of cardiac death or recurrent cardiac events such as myocardial infarction and revascularization procedures.[5, 6]

- Several case series and registry-based studies have reported the outcomes of large numbers of patients treated in a number of different institutions. There are several problems with this kind of evidence. These studies, while contributing to the body of knowledge of EECP, do little to address the efficacy or durability of EECP treatment. The lack of comparison groups makes it impossible to rule out either placebo effect or spontaneous recovery among patients with milder disease.

Other systematic reviews have evaluated EECP for chronic stable angina. In 2010, Amin and colleagues published a Cochrane review of major databases through 2008 on evidence of the effectiveness of EECP for chronic angina pectoris.[12] The solitary RCT identified was the MUST-EECP trial. The authors of this review highlighted patient selection for this study. They comment that limiting the study population to patients with CCS class below IV diminishes the study's generalizability to patients of interest, that is, patients with the most severe symptoms of chronic angina pectoris.

Also in 2010, Shah et al published a meta-analysis of prospective studies, not limited to RCTs, of EECP in stable angina in which CCS class was adequately reported before and after treatment.[13] The MUST-EECP RCT was not included, as change in CCS class was not one of the reported outcomes. A total of 13 studies met these inclusion criteria (n=949 patients). Overall, improvement of at least one level of angina class occurred in 86% of patients (95% confidence interval [CI]: 82-90%, p=0.008). No conclusions can be drawn from this analysis given the lack of randomization (comparison group) for most studies in this analysis.

In 2009, McKenna et al report on a systematic review and economic analysis of EECP for the treatment of stable angina and heart failure.[14] Four studies (one RCT and three non-randomized comparative studies) comparing EECP treatment with no treatment in adults with chronic stable angina were included in the analysis.[1,2,10,11] The systematic review included a study by Barsheshet et al in which 25 patients (15 EECP and 10 controls) were evaluated at the end of treatment.[15] Similar to the previously reviewed Schechter et al(2003) study,[11] "CCS classification improved with EECP but not with usual care, however statistical analysis of between group differences was not reported and, for CCS classification, the data were treated as continuous data which is inappropriate for this four-category classification."

A 2016 systematic review and meta-analysis by Qin et al focused on the effect of EECP on the intermediate measure of myocardial perfusion in patients with CAD.[16] The review included 6 studies reporting on myocardial perfusion or coronary flow outcomes published from 1992 to 2007, including 5 RCTs and 1 prospective, observational, blinded study. In pooled analysis, EECP was associated with increased myocardial perfusion in CAD patients (pooled weighted mean difference, -0.19; 95% CI, -0.38 to 0.00; p=0.049).

Registry Studies

Registry-based studies have been published that report on relatively large numbers of patients. In a registry-based study by Soran et al (2007), 450 patients with left ventricular dysfunction (ejection fraction, EF ≤40) and refractory angina had 0.7

fewer emergency department visits and 0.8 fewer hospitalizations 6 months after treatment with EECP compared to the 6 months before EECP; 6-month data were available on only 81 patients.[17] Drawing conclusions from this study is not possible due to lack of a comparison group.

Another registry-based study (the International Enhanced External Counterpulsation Patient [IECP] Registry) reported by Loh et al (2008), provided long-term (3-year) results on patients with chronic refractory angina for patients in this registry.[18] The registry enrolled 5,000 patients from 99 U.S. and 9 international centers between 1999 and 2001. However, analysis was completed only for those centers that had at least 80% compliance with follow-up data submission; the study reported results on 1,427 patients. In this selective group, 220 patients (15.4%) died, while 1,061 patients (74.4%) completed their follow-up. Immediately post-EECP, the proportion of patients with severe angina (Canadian Cardiovascular Angina Classification [CCS] III/IV) were reduced from 89% to 25%, $p<0.001$. This was sustained in 74% of the patients during follow-up. More severe baseline angina and a history of heart failure or diabetes were independent predictors of unfavorable outcome. Again, the lack of a control group precludes drawing conclusions about this technology based on this study.

The IECP data have also been examined to determine the safety and efficacy of the use of this device in patients with peripheral arterial disease. Peripheral arterial disease, while a common co morbidity of coronary artery disease, has been regarded as a relative contraindication to EECP due to concerns of compression on peripheral blood flow and a potentially greater risk of aortic rupture. Thakker and colleagues compared registry data in patients with peripheral arterial disease to those who did not.[19] Based on a reduction of one or more CCS angina classes, patients with peripheral arterial disease had a similar rate (76.6% vs. 79.0%, respectively; $p=0.27$) of improvement as did the group without peripheral arterial disease. Rates of hospitalization for all cardiac causes (6.1% vs. 4.4%, respectively; $p=0.17$) and for unstable angina (5.4% vs. 3.5%, respectively; $p=0.25$) were also similar between groups.

Observational Studies

Numerous individual observational studies have been detailed in previous reviews and are included in systematic reviews described above.[2,5,10,11,15,20] For example, two prospective cohort studies (n=55 and n=61) with 1-year outcomes have been reported.[21,22] Improved CCS classification was the main reported outcome, which persisted for 1 year in 79% and 78% of patients in the respective studies. Both studies had higher rates of treatment completion and follow-up than the previously reported (registry) studies assessing long-term outcomes.

Section Summary: Chronic Stable Angina

The data for use of EECP in chronic stable angina is low, making it difficult to form conclusions on the efficacy of this treatment. The single randomized trial (MUST-EECP) that included relevant clinical outcomes reported a benefit on 1 of 4 main angina-related outcomes, and the magnitude of this benefit was of uncertain clinical significance. The RCTs that report on intermediate outcomes offer evidence on possible physiologic mechanisms underlying EECP treatment. A 2016 metal-analysis included 5 RCTs and 1 prospective, observational, blinded study. In pooled

analysis, EECP was associated with increased myocardial perfusion in CAD patients. Observational studies, such as registry data and case series, offer modest evidence on the efficacy of this procedure.

HEART FAILURE

Review of Evidence

The 510(k) approval of the Vasomedical devices states that objective measures such as peak oxygen consumption, exercise duration, and pre-load-adjusted maximal left ventricular power are improved following EECP therapy, as well as subjective measures of patient response to therapy, such as quality of life and functional ability measures.[23] However, no clinical details of these studies are provided in the FDA summary, and these data are not from controlled trials.

The 2005 TEC Assessment included heart failure in the analysis and concluded the evidence supporting the role of EECP as an effective treatment for heart failure is lacking in both quantity and quality.[9] A single randomized, multicenter study of EECP compared to usual care in 187 optimally medically managed patients with New York Heart Association (NYHA) functional class II or III heart failure with EF ≤35% of ischemic or idiopathic etiology, the "Prospective Evaluation of EECP in Congestive Heart Failure" (PEECH trial), was mostly inconclusive.[24] The design and methods of the PEECH trial were published by Feldman et al (2005).[23] The results of the PEECH trial found statistically improved, but modest, changes in exercise duration and improved functional classification but not in quality of life or peak oxygen uptake (Vo_2).[24]

A 2006 subgroup analysis from the PEECH trial for CHF was published. It showed that subjects aged 65 years and older treated with EECP (n=41) were more likely to meet the exercise duration (35% vs. 25% increased by ≥60 seconds) and peak Vo_2 (30% vs. 11% increased by ≥1.25 ml/kg per min) improvement thresholds compared to those undergoing sham treatment (n=45); there was no difference at 6 months in NYHA class.[25]

In 2015, Rampengan et al reported on a double-blinded RCT evaluating EECP in patients with CHF treated in Indonesia.[26] Patients with NYHA functional class I or II symptomatic heart failure from various causes were included. Patients were randomized to active EECP (n=56) or sham EECP (n=56), which involved the use of the EECP device at only 77 mm Hg of pressure versus the standard 300 mm Hg. Analysis was per protocol, excluding 6 and 7 patients who dropped out of the active and sham groups, respectively. Post intervention, active EECP group patients were more likely to have a 6-minute walk test (6MWT) distance of 300 meters or greater (98.0% vs. 32.7%, $p<0.01$). The change in 6MWT distance was greater (improved) for the active EECP patients (192.6 meters) than for the sham control patients (-9 meters; $p<0.05$).

A small, open-label, ongoing RCT conducted in Russia by Belenkov et al (2024) randomized patients with ischemic heart disease and heart failure to optimal drug therapy alone (n=40), optimal drug therapy plus 1 course of EECP per year (n=40), or optimal drug therapy plus 2 courses of EECP per year (n=40).[27] The total duration is anticipated to be 3 years. At 12 months, the percentage of patients achieving at

least a 20% increase in 6-minute walk test was greater in the EECP groups than optimal drug therapy alone (97.5% and 72.5% vs 7.7%). Longer-term follow-up from this ongoing study may help clarify the role of EECP.

Similar to the registry evidence for EECP for angina, registry studies for heart failure have provided relatively little insight into the comparative efficacy of EECP.[28-31] The single-arm study by Soran et al indicated that patients showed some improvements, but the lack of a comparison arm precludes inferences about the true effects of therapy.[32]

The previously described 2009 review by McKenna et al[14] included the single trial of EECP for heart failure included in the systematic review, the PEECH study.[24] The authors conclude that the studies do not provide firm evidence of the clinical effectiveness of EECP in refractory stable angina or in heart failure and that high quality studies are required to investigate the benefits of EECP and whether these outweigh the common adverse effects.

Section Summary: Heart Failure
The evidence for the use of EECP in heart failure includes 2 RCTs that was reported on clinical outcomes. One study reported modest improvements for some outcomes and no improvement on others. A second study reported improvements in the 6MWT, but has methodologic limitations that limit conclusions that can be drawn. The observational studies added little to the evaluation of efficacy due to the variable natural history of heart failure, the multiple confounding variables for cardiac outcomes, and the potential for a placebo effect. Further high-quality RCTs are needed to determine whether EECP is a useful treatment for heart failure.

OTHER CONDITIONS RELATED TO ISCHEMIA OR VASCULAR DYSFUNCTION

Review of Evidence
The use of EECP for other conditions of ischemia has been investigated. Lin et al 2023 evaluated interventions for central retinal artery occlusion in a Cochrane review.[32] The authors identified one prospective study[33] that failed to find benefit in retinal reperfusion or visual acuity when EECP was added to hemodilution.[33]

Published registry studies also demonstrated improvements in erectile function.[34] Erectile function was improved in a study of 120 men prospectively enrolled from 16 centers. Three of five domains of the International Index of Erectile Function were statistically improved with EECP treatment (erectile function, intercourse satisfaction, and overall satisfaction), and the total score improved from 28 to 32, a statistically significant improvement. The non-comparative design of this study makes it difficult to draw conclusions on treatment efficacy. This indication is added as investigational due to lack of adequate data on clinical outcomes.

Preliminary studies from Asia are also reporting early results on use of EECP to the lower extremities in the treatment of acute ischemic stroke.[35] A 2012 Cochrane review of two RCTs of EECP in acute ischemic stroke concluded that the methodological quality of the studies was poor and reliable conclusions could not be reached from this evidence.[36]

In 2016, Sardina et al reported on an RCT that randomized 30 patients with type 2 diabetes in a 2:1 ratio to EECP (n=20) or standard care for diabetes (n=10), and reported results out to 3 months[37] and 6 months.[38] At 6-month follow-up, patients in the EECP group had significant decreases over time in variety of biomarkers of advanced glycation end products, inflammation, and oxidative stress. At 6-month follow-up, the percent change in advanced glycation end products and receptor of advanced glycation end products differed significantly between groups ($p<0.05$).

Section Summary: Other Conditions Related to Ischemia or Vascular Dysfunction

Two RCTs have assessed use of EECP for treatment of central retinal artery occlusion; both trials had methodologic limitations. Registry studies of erectile function have reported improvements for some outcomes with ECCP but design shortcomings limit conclusions drawn. EECP has also been used to treat acute ischemic stroke, but the evidence base is not robust. EECP has been used in a small RCT to treat type 2 diabetes. Reported follow-up was short-term.

SUMMARY OF EVIDENCE

For individuals who have chronic stable angina who receive enhanced external counterpulsation (EECP), the evidence includes randomized controlled trials (RCTs), observational studies, and systematic reviews. Relevant outcomes are overall survival, symptoms, morbid events, and functional outcomes. There is only 1 blinded RCT that includes clinical outcomes, and it reported benefit on only 1 of 4 main angina outcomes. Additional small RCTs have reported changes in physiologic measures associated with EECP Observational studies, including registry studies with large numbers of patients, add to determinations of efficacy. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have heart failure who receive EECP, the evidence includes RCTs, observational studies, and systematic reviews. Relevant outcomes are overall survival, symptoms, morbid events, and functional outcomes. One RCT that reported on clinical outcomes found a modest benefit with EECP on some outcomes and no benefit on others. A second RCT reported improvements on the 6-minute walk test with EECP, but had methodologic limitations that limit conclusions that can be drawn. The observational studies on EECP in heart failure have limited ability to inform the evidence on EECP due to the multiple confounding variables for cardiac outcomes and the potential for a placebo effect. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have other conditions related to ischemia or vascular dysfunction who receive EECP, the evidence includes RCTs, registry studies, and systematic reviews. Relevant outcomes are overall survival, symptoms, morbid events, and functional outcomes. An RCT assessed use of EECP for treatment of central retinal artery occlusion. Registry studies of erectile function have reported improvements for some outcomes with ECCP but design shortcomings limit conclusions drawn. EECP has also been used to treat acute ischemic stroke, but the evidence base in is not robust. EECP has been used in a small RCT to treat type 2

diabetes. Reported follow-up was short term. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Ongoing and Unpublished Clinical Trials

A search of ClinicalTrials.gov did not identify any ongoing or unpublished trials that would likely influence this review.

SUPPLEMENTAL INFORMATION

Clinical Input Received From Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, BCBSA received input from three academic medical centers while this policy was under review, one during review in April 2008, one during review in October 2008, and one during review in 2009. Reviewers agreed with the conclusion that this was investigational. Some reviewers commented about potential use in those with angina not amenable to surgical interventions.

PRACTICE GUIDELINES AND POSITION STATEMENTS

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

Joint Guidelines from the American College of Cardiology Foundation, American Heart Association et al

The 2012 American College of Cardiology/American Heart Association (ACC/AHA) guidelines on the management of patients with stable ischemic heart disease indicate EECP "may be considered for relief of refractory angina." This recommendation is based on Class IIb, Level of Evidence: B, which indicates the efficacy of the intervention is not well established and further studies would be helpful.[39]

In 2014, ACC/AHA updated to these joint guidelines. Based on their review, the recommendation on EECP remains unchanged from the 2012 guideline.[40]

Government Regulations
National:

NCD Manual 100-3, Chapter 1, part 1. External Counterpulsation Therapy for Severe Angina. Effective date: 3/20/2006. (Rev.50, Issued: 3/31/06, implementation: 04/03/06). Section 20.20.

Effective for services performed on or after July 1, 1999, coverage is provided for the use of ECP for patients who have been diagnosed with disabling angina (Class III or Class IV, Canadian Cardiovascular Society Classification or equivalent classification) who, in the opinion of a cardiologist or cardiothoracic surgeon, are not readily amenable to surgical intervention, such as PTCA or cardiac bypass, because:

1. Their condition is inoperable, or at high risk of operative complications or post-operative failure;
2. Their coronary anatomy is not readily amenable to such procedures; or
3. They have co-morbid states that create excessive risk.

A full course of therapy usually consists of 35 one-hour treatments, which may be offered once or twice daily, usually 5 days per week. The patient is placed on a treatment table where their lower trunk and lower extremities are wrapped in a series of three compressive air cuffs, which inflate and deflate in synchronization with the patient's cardiac cycle.

During diastole, the three sets of air cuffs are inflated sequentially (distal to proximal) compressing the vascular beds within the muscles of the calves, lower thighs and upper thighs. This action results in an increase in diastolic pressure, generation of retrograde arterial blood flow and an increase in venous return. The cuffs are deflated simultaneously just prior to systole, which produces a rapid drop in vascular impedance, a decrease in ventricular workload and an increase in cardiac output.

The augmented diastolic pressure and retrograde aortic flow appear to improve myocardial perfusion, while systolic unloading appears to reduce cardiac workload and oxygen requirements. The increased venous return coupled with enhanced systolic flow appears to increase cardiac output. As a result of this treatment, most patients experience increased time until onset of ischemia, increased exercise tolerance, and a reduction in the number and severity of anginal episodes. Evidence was presented that this effect lasted well beyond the immediate post-treatment phase, with patients symptom-free for several months to two years. This procedure must be done under direct supervision of a physician.

Nationally Non-Covered Indications

All other cardiac conditions not otherwise specified as nationally covered for the use of ECP remain nationally non-covered.

Local:

There is no local coverage determination on this topic.

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

N/A

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The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through June 2024, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
11/13/02	11/13/02	11/13/02	Joint policy established
6/24/04	6/24/04	6/30/04	Routine maintenance
11/1/06	8/25/06	7/31/06	Routine maintenance
11/1/09	8/18/09	8/18/09	Routine maintenance
9/1/12	6/12/12	6/19/12	Routine maintenance. No change in policy statement. Policy reformatted to match the BCBSA policy.
3/1/14	12/10/13	1/6/14	Routine maintenance
11/1/15	8/18/15	9/14/15	Routine maintenance
11/1/16	8/16/16	8/16/16	Routine policy maintenance
11/1/17	8/15/17	8/15/17	Updated rationale section. Added reference # 12, 17, 26, 37 and 38. No change in policy status.
11/1/18	8/21/18	8/21/18	Routine policy maintenance. No change in policy status.
11/1/19	8/20/19		Routine policy maintenance. No change in policy status.
11/1/20	8/18/20		Routine update to policy, no change in policy status.
11/1/21	8/17/21		Routine policy maintenance, no change in policy status
11/1/22	8/16/22		Routine policy maintenance, no change in policy status.
11/1/23	8/15/23		Routine policy maintenance, no change in policy status. Vendor managed: N/A. (ds)
11/1/24	8/20/24		Updated rationale, added references 27 & 32, removed reference 41. Vendor managed: N/A (ds)

Next Review Date: 3rd Qtr. 2025

Pre-Consolidation Medical Policy History

Original Policy Date	Comments
BCN: 6/28/01	Revised: N/A
BCBSM: 3/3/01	Revised: N/A

BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: ENHANCED EXTERNAL COUNTERPULSATION (EECP)

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Covered; criteria apply
BCNA (Medicare Advantage)	See government section
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.