Anthem

Medical Policy

Subject: Carotid Sinus Baroreceptor Stimulation Devices
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Description/Scope

This document addresses the insertion and use of a carotid sinus baroreflex activation device which has been proposed for the treatment of drug-resistant hypertension and heart failure.

Position Statement

Investigational and Not Medically Necessary:

The use of a carotid sinus baroreflex activation device is considered **investigational and not medically necessary** for all indications.

Rationale

Description of Technology
Electrical activation of the carotid sinus baroreflex was first introduced in the 1960s and 1970s. It consists of chronically stimulating the carotid sinus nerves using implanted nerve electrodes with an implantable radiofrequency controlled receiver. The devices bilaterally activate the carotid sinus baroreflex by electrically stimulating the carotid sinus wall. A surgical implant procedure is used to place the device under the skin near the clavicle. The electrodes are placed on the carotid arteries and the leads run under the skin and are connected to a battery powered implanted impulse generator device.

Conditions
Hypertension

In 2014, the Barostim neo® Legacy System (CVRx, Inc., Minneapolis, MN) received Humanitarian Device Exemption (HDE) from the U.S. Food and Drug Administration (FDA). The device is indicated for use in individuals with resistant hypertension who had bilateral implantation of the Rheos® carotid sinus leads, which have been discontinued and are considered obsolete, and were determined responders in the Rheos pivotal clinical study. The HDE approval process is applicable to devices intended to benefit individuals in the treatment or diagnosis of conditions or diseases that affect fewer than 4000 individuals in the U.S. per year. An HDE application is not required to submit the results of scientifically valid clinical investigations demonstrating the effectiveness of the device for its intended use. However, the application must contain sufficient information for the FDA to determine that the device does not pose an unreasonable or significant risk of illness or injury and that the probable health benefit outweighs the risks from its use. In addition to the Barostim neo, additional devices using baroreceptor response in the carotid sinus to stimulate vasodilation are being studied.

Drug-resistant hypertension is diagnosed when blood pressure remains above goal despite the use of three concurrent antihypertensive agents of different classes. Of the three agents, one should be a diuretic and all of them should be prescribed at their optimal dose amounts. The number of individuals with drug-resistant hypertension is unknown but is estimated to be 20% to 30% of clinical trial participants with the prevalence expected to increase due to the aging of the population. Drug-resistant hypertension is not the same as uncontrolled hypertension. Uncontrolled hypertension is a lack of blood pressure control due to poor adherence or an insufficient treatment regimen.

Other treatment options are being explored to treat drug-resistant hypertension. Activation of the carotid sinus baroreflex was first introduced for the treatment of drug-resistant hypertension and refractory angina pectoris. Blood pressure lowering is felt to be mediated through sympathetic inhibition (Heusser, 2010). This approach was not adopted as a viable treatment option for hypertension due to the development of new drugs used in the treatment of hypertension and the technical limitations of implantable medical devices. Newer devices are now being developed and studied.

Tordoir and colleagues (2007) report on the preliminary analysis of 17 participants with drug-resistant hypertension. During this study the participants' antihypertensive regimens remained the same for the first 4 months. The participants were analyzed at the 4-month follow-up (3 months following the continued electrical baroreflex activation therapy). Investigators hypothesized that there would be a reduction of at least 10 mm Hg of systolic blood pressure at the 4-month follow-up. Adverse events related to the device included intraoperative bradycardia and pain. Adverse events related to the procedure included infection, hypoglossal nerve injury, intraoperative bradycardia, pain, wound complication, extravascular tissue stimulation, anesthesia complications, and injury to local tissue. One-month systolic blood pressure (prior to device activation) ranged from 144-184 and diastolic blood pressure ranged from 84-105. At 4 months, systolic blood pressure ranged from 143-165 and diastolic blood pressure ranged from 81-95. The investigators also reported that "the degree of hemodynamic change was directly related to the amplitude of stimulation." The authors concluded that the preliminary data suggest reasonable safety of the implant and sustained hemodynamic response up to 4 months. However, the authors further noted that "long-term therapeutic results of this ongoing safety and efficacy trial are needed as the basis for a multi-center, controlled trial of the device for this indication" (Tordoir, 2007).

Scheffers and colleagues (2010) reported on the safety and efficacy of an implantable device for use in drug-resistant hypertension. The Device Based Therapy in Hypertension Trial (DEBuT-HT) studied 45 participant over a 3-month time period for the safety and efficacy of the carotid sinus baroreflex activation device. Blood pressure of the participants was greater than or equal to 160/90 despite the use of at least three antihypertensive medications (one of which was a diuretic). All participants were deemed compliant with their medication regimen and the regimen was kept constant for 2 months prior to entering the study. The study baseline time point was 1 month following insertion of the device which is when the device was activated. Participants were followed monthly for the first 3 months and annually thereafter. Of the 45 participants who received the implanted device, the first 3 participants were excluded from the analysis per protocol of the study. Four participants dropped out of the study and 1 missed visits resulting in 37 participants available for evaluation. At the 3-month office evaluation, systolic blood pressure decreased by 21 mm Hg and diastolic blood pressure decreased by 12 mm Hg. Twenty-six participants were evaluated at 1 year. At that time, systolic blood pressure decreased by 30 mm Hg and diastolic blood pressure decreased by 20 mm Hg. At the 2-year visit, only 17 participants were available for evaluation. Systolic blood pressure decreased by 33 mm Hg and diastolic blood pressure decreased by 22 mm Hg.

Bisognano (2011) reported the results of the Rheos Pivotal trial, which was a randomized, double-blind, placebo-controlled study to

measure safety and efficacy of a baroreflex activation device for individuals with drug-resistant hypertension. A total of 265 individuals met enrollment criteria which consisted of systolic blood pressure ≥ 160 mm Hg with diastolic blood pressure ≥ 80 mm Hg. At least 1 month of maximally tolerated therapy with at least three antihypertensive medications (including a diuretic) was completed before the next blood pressure reading. After 1 month of drug therapy, participants were randomized into 2 groups; Group A consisted of 181 individuals who received immediate implant of a baroreflex activation device. Group B was 84 individuals who received the implant of a baroreflex activation device following a 6-month deferment. Primary endpoints were: 1) acute efficacy; 2) sustained efficacy; 3) procedure safety; 4) baroreflex activation therapy safety; and 5) device safety. Secondary endpoints included mean change of systolic blood pressure and a comparison of immediate versus deferred efficacy. In order to maintain blinding, statistical analyses were completed by a data monitoring committee. At the 6-month analysis, 95 participants had not yet completed their 6-month visit and the committee advised that it was unlikely the trial would attain significance for the acute efficacy analysis. The trial also failed to meet the endpoint for procedure safety with an event-free rate of 74.8% which was less than the pre-specified criterion of 82%. The majority of events were related to the carotid sinus lead placement, but also included general surgical complications, respiratory complaints, and wound complications. The mean change in systolic blood pressure decreased by 16 ± 29 mm Hg at 6 months for Group A and 9 ± 29 mm Hg for Group B. At 12 months (in which Group A had received 12 months of baroreflex activation therapy) the mean systolic blood pressure decrease was 25 ± 32 mm Hg, Group B had received 6 months of baroreflex activation therapy at the 12-month visit and their mean systolic blood pressure decrease was 25 ± 31 mm Hg.

Bakris and colleagues (2012) reported on the long-term follow-up of the Rheos Pivotal Trial. Several individuals from the Rheos trial participated in a single-arm, open-label, non-randomized continuation study to assess safety and efficacy of baroreflex activation therapy at 12 months. There were 276 participants from the original Rheos trial that remained in the continuation trial. These participants were measured for clinically significant response as measured by a systolic blood pressure less than or equal to 140 mm Hg (less than 130 mm Hg in diabetics or those with renal disease) or if systolic blood pressure dropped by 20 mm Hg or more from device activation. A total of 244 of the 276 participants were classified as clinically significant responders. The status of 32 participants is as yet undetermined. At month 12, systolic blood pressure dropped more than 30 mm Hg from the preimplantation to the low 140s with an average systolic blood pressure of 143 mm Hg. There have been 13 deaths throughout the course of the trial, none of which were judged to be related to either the procedure or the device. The longer term follow-up shows great potential of baroreflex activation therapy in the treatment of resistant hypertension. However, there are limitations including dilution of statistical power by the high observed variability in blood pressure measurements and the hampering by baseline levels of and adjustments to aggressive medical therapy. Future studies with stable background therapies and fewer confounding therapies are reasonable and the strength of conclusions is limited by the exclusion of the participants deemed to be nonresponders.

A second generation device has also been developed. Hoppe and colleagues (2012) reports on 30 participants with resistant hypertension with a systolic blood pressure greater than or equal to 140 mm Hg. The primary efficacy objective was a reduction in systolic blood pressure through 6 months of baroreflex activation therapy. The primary safety objective was description of all complications though the 6 months of therapy. Baroreflex activation therapy was initiated 2 weeks after being implanted. One participant missed their 6-month visit and data was collected for 29 participants at 6 months. Preimplant baseline blood pressures were 171.1 ± 20.2/99.5 ± 13.9 mm Hg. Postimplant systolic blood pressure was reduced by an average of 26.1 ± 3.3 mm Hg and remained stable at the 6-month visit. Complications included a self-inflicted wound complication, a pulse generator pocket hematoma, and discomfort in the pulse generator pocket which prompted the request to have the device repositioned. Larger scale, randomized controlled trials with long-term follow-up are necessary to evaluate efficacy and safety of baroreflex activation therapy.

In a 2016 prospective trial by Wallbach and colleagues, the authors evaluated the impact of the second generation baroreflex activation therapy device on 24-hour ambulatory blood pressure in those individuals with hypertension refractory to therapy. Study inclusion criteria included office systolic blood pressure greater than or equal to 140 mm Hg or greater than or equal to 130 mm Hg for those individuals with chronic kidney disease and proteinuria, therapy of at least three antihypertensive medications including a diuretic, and age greater than or equal to 18 years. All study participants had been treated for hypertension for at least 1 year and baseline medication was unchanged for at least 3 months prior to implantation of the device. A total of 51 participants were included in the study, however 7 participants were excluded from analysis due to missing or insufficient follow-up ambulatory blood pressure data. All participants had ambulatory blood pressure performed prior to implantation of the baroreflex activation therapy device and at 6 months after initiation of the therapy device. Adverse events included 1 participant with contralateral stroke and 10 participants with procedure-related complications including disturbance of wound healing, post-operative hematoma, hematoma of the vocal cord, repositioning and revision surgeries. There was a drop in systolic blood pressure of greater than or equal to 10 mm Hg in office or greater than or equal to 5 mm Hg in ambulatory blood pressure in 34 of 44 participants. The withdrawal of at least one antihypertensive drug was realizable in 16 participants and 10 participants had antihypertensive treatment increased. This study has limitations which includes lack of a control group which according to the authors would be “crucial in defining real outcomes.” It is also noted that the study inclusion criteria for blood pressure was readings taken during the office and not ambulatory readings. While this approach holds promise for those individuals with drug-resistant hypertension, further clinical trials are necessary to establish the safety and durable benefit of the device.

de Leeuw and colleagues (2017) reported on the results of baroreceptor activation therapy during a 6-year period. They followed the participants from three trials that evaluated the device-based therapy: (the US Rheos Feasibility Trial [Illig. 2006], the DEBuT-HT Trial [Scheffers, 2010], and the Rheos Pivotal Trial [Bisognano, 2011]). There were 143 participants who completed the 5-year follow-up and 48 participants who were followed for 6 years. In the entire cohort, systolic blood pressure fell over the 6-year period from 179 ± 24 mm Hg to 144 ± 28 mm Hg and diastolic pressure dropped from 103 ± 16 mm Hg to 85 ± 18 mm Hg. Several limitations should be noted. Two of the three studies were not randomized. None of the studies had a control group for comparison during the prolonged follow-up. The data presented relates to office blood pressures only.

In a 2020 observational study, Wallbach and colleagues reported on 60 participants with resistant hypertension who were treated with the baroreflex activation therapy neo device. Follow-up continued for 24 months following the initiation of therapy. Baseline office blood pressure was 172 ± 25/90 ± 17 mm Hg. There were 50 participants available for analysis at the 2-year follow-up. Reduction of in-office blood pressure measurements at 24 months was–25 ± 33/–9 ± 18 mm Hg. After 24 months, the number of antihypertensive medications was reduced to a median of 5 from a baseline median of 7. There were 46 participants available for 2-year follow-up of 24-hour ambulatory blood pressure. Baseline 24-hour ambulatory blood pressure was 150 ± 16/80 ± 12 mm Hg with a reduction of –8 ± 23/–5 ± 13 mm Hg after 24 months. The major limitations of the study are the small sample size and lack of randomization with a control group. The authors conclude “Therefore, there is a strong need for randomized controlled trials to determine whether the effect is due to BAT rather than a placebo or nontreatment effect over time.”

A 2018 systematic review and meta-analysis by Chunbin and colleagues reported on studies that assessed the use of baroreflex activation therapy as a treatment for individuals with resistant hypertension. Studies included were randomized controlled trials (n=1) or prospective non-randomized controlled trials (n=11) which evaluated the safety and efficacy of baroreflex activation therapy for resistant hypertension. These 12 studies were eligible for qualitative analysis and 5 of the prospective studies were selected for meta-analysis. The 5 prospective studies compared systolic and diastolic blood pressure for individuals who received baroreflex activation therapy in the hospital. Follow-up ranged from 3-24 months. The conclusions were that both systolic and diastolic blood pressure was decreased by baroreflex activation therapy. Five studies reported on the safety of baroreflex activation therapy. Following use of the

Rheos system, there were 68 procedure adverse events and 34 device adverse events. The second-generation Barostim neo device had a reported three procedural complications. While the studies which analyzed the use of baroreflex activation therapy showed a decrease in systolic and diastolic blood pressure, the sample sizes in the studies were small. There was only one randomized controlled trial obtained suggesting a risk of bias. None of the studies compared the use of baroreflex activation therapy to anti-hypertensive drug treatment. There were different follow-up times across the studies. The authors concluded:

> There is currently insufficient evidence to make firm categorical statements on the efficacy and safety of BAT for the treatment of patients with Resistant Hypertension. However, BAT is a promising treatment for resistant hypertension, but further high-quality RCTs with long-term follow-up is required for a full evaluation.

Another 2018 systematic review and meta-analysis by Wallbach and colleagues reported on 9 studies (7 observational and 2 randomized) with a total of 444 participants. Following baroreflex activation therapy, the studies showed a reduction of systolic blood pressure of -36 mm Hg (95% confidence interval [CI], -42 to -30 mm Hg). An analysis of the short-term (1–6months) effects showed a reduction of -21 mm Hg (95% CI, -26 to -7 mm Hg) and long-term effects (≥ 12months) showed a reduction of –38 mm Hg (95% CI, -46 to -30 mm Hg). While this meta-analysis of baroreflex activation therapy showed reduction of systolic blood pressure, there are very few controlled trials and according to the authors, “data need to be interpreted with caution.” Further randomized controlled trials with well-defined endpoints are necessary to assess safety and efficacy due to the significant number of individuals who suffer from resistant hypertension.

The American College of Cardiology published guidelines in 2017 for high blood pressure in adults. Their recommendation is that while studies are investigating devices that interrupt sympathetic nerve activity, “these studies have not provided sufficient evidence to recommend the use of these devices in managing resistant hypertension.”

Heart Failure
In addition to hypertension, baroreflex activation therapy has also been proposed as a treatment for heart failure.

In 2019, the FDA granted Breakthrough Device designation to the Barostim neo system for the improvement of symptoms of heart failure. As discussed above, baroreflex activation therapy is accomplished by inserting an electrode to the carotid artery. The electrode is attached to an implantable pulse generator device which is inserted under the skin below the clavicle. It delivers an electrical stimulation through the lead. As a basis for the FDA decision, the Baroreflex Activation for Heart Failure (BeAT-HF) (NCT02627196) trial was cited (FDA, 2019). It was a prospective, randomized, open-label trial in which 480 individuals with reduced ejection fraction heart failure were randomized to receive either baroreflex activation therapy with medical management or medical management alone. Participants will be followed for at least 12 months and assessed for safety and efficacy of baroreflex activation therapy. The trial was designed in two phases: expedited and extended. The FDA approval was based on the expedited phase results. The primary endpoints were assessed at 6 months and included the major adverse neurological and cardiovascular events (MANCE) event-free rate for the device arm only must be greater than 85%, the 6-minute hall walk, Minnesota Living With Heart Failure Questionnaire Quality of Life (MLWHFQ QOL or QOL), and N-terminal pro-brain natriuretic peptide (NT-pro-BNP) in the device arm must be statistically better than the medical management only arm. At the 6 month follow-up, the initial cohort of individuals met the 6-minute hall walk distance and quality of life endpoints, but failed to meet the NT-pro-BNP endpoints. The NT-pro-BNP percent change at baseline went from 1096.0 to 809.0 in the device arm and from 1171.0 to 1093.0 in the medical management arm only. In the device arm, there were 125 participants analyzed for MANCE-free rate at 6 months with 118 participants who were MANCE-free showing a rate of 94.4%. For the 6-minute hall walk test, in the device arm 139 baseline participant scores were 294.4 ± 76.4 to 339.0 ± 107.9 for 106 participants at 6 months. In the medical management only arm, with 127 participants analyzed, the 6-minute hall walk test went from 289.5 ± 69.1 to 277.5 ± 111.0. Using the MLWHFQ QOL, at 6 months 107 participants were available and scores went from 55.3 ± 24.1 to 32.3 ± 26.3 in the baroreflex activation therapy plus medical management arm. In the medical management arm only, QOL scores went from 51.3 ± 24.3 to 42.0 ± 25.7 for the 131 participants available for analysis. There were 4 MANCE events: 1 stroke, 1 participant with acute decompensated heart failure, and 2 participants who acquired an infection requiring explant of the device. Out of 125 participants who received the device, 9 participants experienced procedure-related complications within 6 months of implant. The complications included nerve damage/stimulation, respiratory failure, hoarseness, pneumonia, stroke, and thromboembolism. While the post-hoc data appears promising, prospective evaluation of the device has not been duplicated otherwise, and more robust outcomes, such as heart failure-associated healthcare utilization or mortality were not evaluated. The study was published in 2020 by Zile and colleagues.

In 2015, Abraham and colleagues reported on a prospective, randomized, parallel-controlled, clinical trial of 146 individuals with advanced heart failure to assess the safety and efficacy of carotid baroreflex activation therapy. The participants had moderately severe (New York Heart Association [NYHA] functional class III) chronic heart failure with left ventricular ejection fraction of 35% or less. The primary safety objective was to determine the event-free rate of all system- and procedure-related MANCE. The primary efficacy end points were changes in NYHA functional class, quality of life score, and 6-min hall walk distance. There were 70 participants randomized to the control group and 76 participants randomized to baroreflex activation therapy. With an overall MANCE-free rate of 97.2%, and system- and procedure-related complication event-free rate of 85.9%, complications included urinary retention, urinary tract infection, hematoma, bradycardia, atrial arrhythmia, hypotension, worsening heart failure, pneumothorax, and cervical neuralgia. There were 55% of participants in the treatment group that showed at least a 1-class improvement in NYHA functional class compared to 24% in the control group. The between-group difference in quality of life score was -19.5 ± 4.2 points, favoring baroreflex activation therapy with the between-group difference in 6-min hall walk distance was 58.1 ± 19.8 m, also favoring baroreflex activation therapy. With the study outcomes favoring baroreflex activation therapy for heart failure, this study has limitations which include a relatively small number of participants (based on the number of individuals with heart failure). With the lack of participant blinding and a sham control, there is potential for a placebo effect in the treatment arm. There is also potential for bias due to lack of blinding in the investigator assessment of end points. The study did not assess established heart failure clinical outcomes such as heart failure-associated healthcare utilization or mortality.

Using the Abraham 2015 study cohort, Halbach and colleagues (2018) performed a subgroup analysis of the safety and efficacy of baroreflex activation therapy in individuals with and without coronary artery disease. There were 71 participants treated with baroreflex activation therapy. Coronary artery disease was known in 52 of those participants and 19 participants did not have known coronary artery disease. In the control group, 49 participants had known coronary artery disease and 20 participants did not have coronary artery disease. In the treatment group, the system- or procedure-related MANCE rate was 3.8% in the group with coronary artery disease vs. 0% in the group without coronary artery disease. There were no major differences found in the safety or efficacy of those treated with baroreflex activation therapy between the participants with and without coronary artery disease. There was a small number of participants and since the analysis was post-hoc, history of known coronary artery disease was based on medical history, not standardized imaging or functional tests. There may have been participants classified as no coronary artery disease when they did in fact have coronary artery disease. Larger studies are needed.

Using the participant populations from the Abraham, 2015 study and the Zile, 2020 study, Coats and colleagues (Coats, 2022) reported on a meta-analysis to review the efficacy of baroreflex activation therapy. Included participants had NYHA class III or II, a reduced left ventricular ejection fraction (LVEF) ≤35%, and were on guideline-directed medical therapy. In this meta-analysis, 554

participants were included. Efficacy endpoints that were evaluated include the change from baseline to 6 months for 6-min hall walk distance, MLWHF QoL, NYHA class, and N-terminal pro-brain natriuretic peptide (NT-proBNP) for baroreflex activation therapy. At the 6 month follow-up, for the 6-min hall walk distance, those who received baroreflex activation therapy showed a statistically significant improvement over the control group of 48.5 m (95% CI 32.7, 64.2). Quality of life assessed by MLWHF, showed BAT baroreflex activation therapy led to an improvement (shown as a decrease) of −13.4 points (95% CI −17.1, −9.6). Those who received baroreflex activation therapy also showed 3.4 higher odds of improving at least one NYHA class (95% CI 2.3, 4.9) when comparing from baseline to 6 months. The NT-proBNP levels appeared to improve in all participants, but did not reach statistical significance in the cohorts that excluded those with NT-proBNP >1600 pg/ml. While the meta-analysis showed improvement in exercise capacity, QoL, and functional capacity for those who received baroreflex activation therapy, the limitation to only two open-label, randomized trials may have led to bias.

In a 2022 open-label, single-center study, Nottebohm and colleagues reported the results of baroreflex activation therapy on the effect of exercise capacity in 17 individuals with heart failure. Inclusion criteria was NYHA class ≥III, ejection fraction ≤ 35%, and on stable guideline-directed medical and device therapy. There were 12 participants who underwent cardiopulmonary exercise testing before and after administration of baroreflex activation therapy. For those with cardiopulmonary exercise testing results available, peak VO2 was 0.9 (0.57–1.6)l/min at baseline and 1.2 (0.8–1.5)l/min after baroreflex activation therapy. Weight-adapted peak VO2 increased from 10.1 (8.2–12.9) ml/min/kg before baroreflex activation therapy to 12.1 (10.4–14.6) ml/min/kg after treatment. Body weight did not change with 92.5 (85.5–115.3) kg at baseline and 91.0 (82.8–111.8) kg at follow-up (p=0.779). Maximal heart rate was 105 beats per minute at baseline and 114 beats per minute following therapy. Peak oxygen pulse was 10.2 (5.7–13.0) ml/heartbeat at baseline and 10.3 (7.8–15.8) ml/heartbeat at follow-up. There was no significant difference in maximal workload and maximal blood pressure under treatment with baroreflex activation therapy. There were 7 participants who improved from NYHA class III to II and one from NYHA class IV to III at 6 months following baroreflex activation therapy. At 12 months follow-up there was an improvement of 6-min hall walk from 355 (286.8–412.5) m at baseline to 395 (350.3–452.5) m. No effect on quality of life was assessed by MLHFQ score. LVEF was increased from 29.5 (19.5–30) % at baseline to 30.5 (27.8–35.5) % at 12 months. Following baroreflex activation therapy, one participant had the device removed due to local infection, three participants died however there was no association to the baroreflex activation therapy, one participant requested removal of device due to complaint of arm pain, and two participants underwent heart transplants after baroreflex activation therapy. Generalizability of results may not be possible due to the low enrolled number of participants, the open-label design, and lack of control group.

In 2023, Guckel and colleagues reported the results of a prospective study participants with advanced heart failure who received baroreflex activation therapy. Efficacy was measured by an improvement in QoL as measured by (EQ-5D-5L), NYHA class, LVEF, hospitalization rate, NT-proBNP levels, and 6-min hall walk distance. Follow-up visits were performed at 3, 6, and 12 months following implantation of the device. At baseline, the mean LVEF was 27 ± 1%, NYHA was class III, NT-proBNP value averaged 2302 ± 460 pg/mL, the 6-min hall walk distance was 281 ± 23 m. All participants received guideline-directed medical therapy and 15 participants were treated with heart failure medications (angiotensin-receptor neprilysin inhibitor [ARNI]). With an initial study group of 40 participants, 10 participants elected to have baroreflex activation therapy. For those who received baroreflex activation therapy, LEVF increased +10% and improved NYHA class -88%. With the addition of ARNI, LVEF increased 9% with an improved NYHA class -90%. QoL increased 21% with baroreflex activation therapy and 22% with the addition of ARNI. NT-proBNP levels decreased by 24% following baroreflex activation therapy and 37% for those also taking ARNI. Hospitalization rates were lower in the baroreflex activation therapy group compared to the control group. The authors note further randomized studies are necessary to direct guideline recommendations and soft clinical endpoints, for example NYHA class and QoL may be subject to a participant's subjective perception.

A 2023 systematic review by Molina-Linde and colleagues reported the efficacy of baroreflex activation therapy in individuals with heart failure with reduced ejection fraction. The authors included six systematic reviews, two randomized clinical trials, and two economic studies. For analysis of the systematic reviews, the authors note data from different articles use the same participant population with may have overestimated the true effect of baroreflex activation therapy. For the two randomized clinical trials (Abraham, 2015; Zile, 2020), use of baroreflex activation therapy showed improvements in NYHA functional class, QoL, 6-min walk test, and NT-proBNP levels. However, the included studies did not evaluate mortality or changes in cardiovascular structure or function. Improvements should be interpreted with caution as some of the changes were subject to subjective perception (NYHA class and QoL score). The authors conclude "Further studies and long-term follow-up are needed to assess efficacy in reducing cardiovascular events and mortality."

A 2023 retrospective review by Blanco and colleagues reported the impact of baroreceptor activation therapy on the rate of heart failure hospitalization and death. In this study, 30 participants with chronic heart failure with LVEF ≤35% and persistent dyspnea despite optimized medical treatment were included and had been treated with baroreceptor activation therapy. After 12 months of baroreceptor activation therapy, 6 participants died, 3 participants didn't attend follow-up visits. In the remaining 21 participants, blood pressure and heart rate were stable. At baseline, NHYA class was III in 26 participants, IV in 4 participants. At 12 months follow-up, NYHA class improved in 19 participants and remained unchanged in 5 participants. LVEF at baseline was 25.5 (20.0–30.5) % and was 30.0 (25.0–36.0) % at 12 months. There was a nonsignificant numerical decrease in NT-proBNP [3165 (880–8085) vs. 1001 (599–3820) pg/mL]. At 1 year, mortality was 20% (n=6) and 33% (n=10) at 3 years. There were 14 participants who were hospitalized due to heart failure during follow-up. The retrospective, non-blinded, non-randomized design may lead to bias. Observed changes could be unrelated to baroreflex activation therapy due to lack of a control group.

In 2021 the European Heart Rhythm Association updated their guideline for the diagnosis and treatment of acute and chronic heart failure (McDonagh, 2021). They note that while baroreflex activation therapy offers a modest improvement in quality of life and effort capacity, there is currently insufficient evidence "to support specific guideline recommendations for a reduction in mortality or hospitalization for these and a variety of other implantable electrical therapeutic technologies."

In 2022, the American College of Cardiology, American Heart Association and the Heart Failure Society of America published guidelines for the management of heart failure (Heidenreich, 2022). They state trials of device stimulation of baroreceptors have had mixed responses.

Conclusion

While the use of baroreflex activation therapy appears promising for resistant hypertension and heart failure, overall trial populations have short follow-up. Longer term outcomes are necessary and there is a lack of literature regarding improved net health outcomes. Clinical trials are underway.

Background/Overview

Hypertension

Blood pressure is the force of blood against the walls of arteries. It is measured by two numbers: the systolic pressure (when the heart beats) over the diastolic pressure (when the heart relaxes between beats). The numbers are written or expressed with the systolic number over the diastolic number. When blood pressure stays elevated over time it is considered to be high blood pressure.

Blood pressure is considered to be hypertensive (higher than normal) when the systolic number is greater than 130 mm Hg and/or the diastolic number is greater than 80 mm Hg. The American Heart Association (AHA) reports that 76.4 million adults in the United States have been diagnosed with hypertension. Many individuals with hypertension take anti-hypertensive medications to control their blood pressure. Some individuals with hypertension are resistant to the medication. For those who have drug-resistant hypertension other treatment options are being explored; in particular, electrical stimulation of the carotid sinus baroreceptors.

The carotid sinus is an enlarged area in the neck at the point of bifurcation of the carotid artery which contains baroreceptors (pressure receptors). When the baroreceptors are stimulated this causes slowing of the heart rate, vasodilation (widening of the blood vessel) and a decrease in blood pressure.

Heart Failure
The term heart failure refers to the fact the heart isn't pumping as well as it should be. Blood and oxygen is delivered to the body by way of the heart pumping. When the heart is weakened, it cannot supply the body with enough blood which can lead to fatigue and shortness of breath. Treatment of heart failure can include modifications to lifestyle, medications, and devices or surgery. The AHA estimates that approximately 6.2 million persons in the United States have heart failure.

Definitions

Heart failure: A condition in which the heart no longer adequately functions as a pump. As blood flow out of the heart slows, blood returning to the heart through the veins backs up, causing congestion in the lungs and other organs.

Hypertension: The term used to describe high blood pressure.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

When services are Investigational and Not Medically Necessary:
When the code describes a procedure indicated in the Position Statement section as investigational and not medically necessary.

CPT

0266T	Implantation or replacement of carotid sinus baroreflex activation device; total system (includes generator placement, unilateral or bilateral lead placement, intra-operative interrogation, programming, and repositioning, when performed)
0267T	Implantation or replacement of carotid sinus baroreflex activation device; lead only, unilateral (includes intra-operative interrogation, programming, and repositioning, when performed)
0268T	Implantation or replacement of carotid sinus baroreflex activation device; pulse generator only (includes intra-operative interrogation, programming, and repositioning, when performed)
0269T	Revision or removal of carotid sinus baroreflex activation device; total system (includes generator placement, unilateral or bilateral lead placement, intra-operative interrogation, programming, and repositioning, when performed)
0270T	Revision or removal of carotid sinus baroreflex activation device; lead only, unilateral (includes intra-operative interrogation, programming, and repositioning, when performed)
0271T	Revision or removal of carotid sinus baroreflex activation device; pulse generator only (includes intra-operative interrogation, programming, and repositioning, when performed)
0272T	Interrogation device evaluation (in person), carotid sinus baroreflex activation system, including telemetric iterative communication with the implantable device to monitor device diagnostics and programmed therapy values, with interpretation and report (eg, battery status, lead impedance, pulse amplitude, pulse width, therapy frequency, pathway mode, burst mode, therapy start/stop times each day);
0273T	Interrogation device evaluation (in person), carotid sinus baroreflex activation system, including telemetric iterative communication with the implantable device to monitor device diagnostics and programmed therapy values, with interpretation and report (eg, battery status, lead impedance, pulse amplitude, pulse width, therapy frequency, pathway mode, burst mode, therapy start/stop times each day); with programming

HCPCS

C1825	Generator, neurostimulator (implantable), non-rechargeable with carotid sinus baroreceptor stimulation lead(s)

ICD-10 Procedure

03HK0MZ	Insertion of stimulator lead into right internal carotid artery, open approach
03HK3MZ	Insertion of stimulator lead into right internal carotid artery, percutaneous approach
03HK4MZ	Insertion of stimulator lead into right internal carotid artery, percutaneous endoscopic approach
03HL0MZ	Insertion of stimulator lead into left internal carotid artery, open approach
03HL3MZ	Insertion of stimulator lead into left internal carotid artery, percutaneous approach
03HL4MZ	Insertion of stimulator lead into left internal carotid artery, percutaneous endoscopic approach

ICD-10 Diagnosis

	All diagnoses

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Index

The use of specific product names is illustrative only. It is not intended to be a recommendation of one product over another, and is not intended to represent a complete listing of all products available.

Document History

Status	Date	Action
Reviewed	02/15/2024	Medical Policy & Technology Assessment Committee (MPTAC) review. Revised Rationale and References sections.
Reviewed	02/16/2023	MPTAC review. Updated Rationale and References sections.
Reviewed	02/17/2022	MPTAC review. Updated Rationale, Background/Overview, References, and Index sections.
Reviewed	02/11/2021	MPTAC review. Updated Rationale, References and Index sections.
	12/16/2020	Updated Coding section with 01/01/2021 HCPCS changes; added C1825.
Reviewed	02/20/2020	MPTAC review. Added heart failure to scope of document. Updated Description/Scope, Rationale, Background/Overview, Definitions, References and Index sections.
Reviewed	03/21/2019	MPTAC review. Updated Rationale and References sections.
Reviewed	05/03/2018	MPTAC review. The document header wording updated from “Current Effective Date” to “Publish Date.” Updated References section.
Reviewed	05/04/2017	MPTAC review. Updated Rationale and References sections.
Reviewed	05/05/2016	MPTAC review. Removed ICD-9 codes from Coding section.
Reviewed	05/07/2015	MPTAC review. Updated Rationale and References.
Reviewed	05/15/2014	MPTAC review. No change to Position Statement.
Reviewed	05/09/2013	MPTAC review. Updated Rationale, Background/Overview and References.
Reviewed	05/10/2012	MPTAC review. Title change to “Carotid Sinus Baroreceptor Stimulation Devices”. Updated Description/Scope, Rationale, References, and Index.
New	05/19/2011	MPTAC review. Initial document development.

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