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Baroreflex Stimulation Devices

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Disclaimer

Carefully check state regulations and/or the member contract.
Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Coverage

Baroreflex stimulation therapy with a device approved by the U.S. Food and Drug Administration **is considered experimental, investigational and/or unproven** for individuals with heart failure despite the use of maximally tolerated guideline-directed medical and device therapy.

Baroreflex stimulation therapy **is considered experimental, investigational and/or unproven** for all other indications.

Policy Guidelines

None.

Description

Baroreflex stimulation devices provide electrical stimulation of the baroreceptors in the carotid arteries using an implanted device. Activation of the baroreflex inhibits the sympathetic nervous system, resulting in various physiologic changes, including slowed heart rate and lower blood pressure.

Background

Baroreceptors are pressure sensors contained within the walls of the carotid arteries. They are part of the autonomic nervous system that regulates basic physiologic functions such as heart rate and blood pressure. When these receptors are stretched, which occurs with increases in blood pressure, the baroreflex is activated. Activation of the baroreflex signals the brain, which responds by inhibiting sympathetic nervous system output and increasing parasympathetic nervous system output. The effect of this activation is to reduce heart rate and blood pressure, thereby helping to maintain homeostasis of the circulatory system.

The use of baroreflex stimulation devices (also known as baroreflex activation therapy) is a potential alternative treatment for heart failure. Heart failure is a relatively common condition, and are initially treated with medications and lifestyle changes. A substantial portion of patients are unresponsive to conventional therapy and treating these patients is often challenging, expensive, and can lead to adverse events. As a result, there is a large unmet need for additional treatments.

Regulatory Status

In 2014, the Barostim Neo™ Legacy System received a humanitarian device exemption from the U.S. Food and Drug Administration for use in patients with treatment-resistant hypertension who received Rheos® Carotid Sinus leads as part of the Rheos pivotal trial and were considered responders in that trial. (1) The Rheos device did not receive FDA approval, and no additional patients will be accrued under the humanitarian device exemption. Barostim is no longer marketed for individuals with treatment-resistant hypertension, and this indication is not presented in this policy.

In 2019, Barostim Neo was granted premarket approval (PMA P180050) and is indicated for the improvement of symptoms of heart failure (i.e., quality of life, six-minute hall walk, and functional status) for patients who remain symptomatic despite treatment with guideline-directed medical therapy, are New York Heart Association (NYHA) Class III or Class II (with a recent history of Class III), and have a left ventricular ejection fraction less than or equal to 35% and a N-terminal pro-B-type natriuretic peptide (NT-proBNP) less than 1600 pg/ml, excluding patients indicated for Cardiac Resynchronization Therapy according to the American Heart Association/American College of Cardiology/European Society of Cardiology guidelines.

It was the first device to be granted approval via the Expedited Access Pathway. (2, 3) The Expedited Access Pathway was a mechanism used to hasten the approval of novel therapies that target life-threatening conditions. The Expedited Access Pathway was subsequently replaced by the Breakthrough Devices Program.

In 2023, following the extended phase of the BEAT-HF study, Barostim Neo's indication was expanded for patients who are NYHA Class III or Class II (who had a recent history of Class III) despite treatment with guideline-directed medical therapies (medications and devices), have a left ventricular ejection fraction of ≤ 35%, and a NT-proBNP <1600 pg/ml. (4)

Rationale

Medical policies 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. Randomized controlled trials 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.

Treatment-Resistant Heart Failure

Clinical Context and Therapy Purpose

The purpose of baroreflex stimulation devices is to provide a treatment option that is an alternative to or an improvement on existing therapies, such as medical therapy in individuals with treatment-resistant heart failure.

The following PICO was used to select literature to inform this policy.

Populations

The relevant population of interest is individuals with treatment-resistant heart failure.

Interventions

The therapy being considered is baroreflex stimulation (also known as baroreflex activation therapy). Implanted devices provide electrical stimulation of the baroreceptors in the carotid

arteries. Activating the baroreflex inhibits the sympathetic nervous system, causing various physiologic changes, including lowering blood pressure (BP).

Comparators
Comparators of interest include optimal medical therapy, implantable devices, and transplantation.

Outcomes
The general outcomes of interest are OS, functional outcomes, quality of life, hospitalizations, medication use, and treatment-related morbidity.

Available literature has followed individuals for up to 3.6 years, but in practice, patients with treatment-resistant heart failure would be followed by cardiologists for the rest of their lives.

The HFC-ARC (Heart Failure Collaboratory and the Academic Research Consortium) expert panel published their findings on using functional and symptomatic clinical trial endpoints in the trial for heart failure. (5) Patient-reported outcomes (PRO) that have been comprehensively evaluated and most used in heart failure trials include the Kansas City Cardiomyopathy Questionnaire (KCCQ-12) and Minnesota Living With Heart Failure Questionnaire (MLHFQ). As therapeutic endpoints, these instruments complement assessment of major adverse cardiac events (MACE). However, their interpretation is complicated by difficulty in determining what change constitutes a minimal clinically important difference (MCID). A treatment effect on such measures that is undetectable by patients has no clear clinical or regulatory utility. The published MCIDs for the KCCQ and MLHFQ are 5 points; however, alternative MCIDs have been reported, and there is limited information on between group changes and durability of effect. (6-10) Responder analyses, in which benefit is defined by an individual's improvement in PRO score crossing a threshold, can assist with interpretation of PRO endpoints; however, they are best avoided as primary analyses because they discard clinical information and statistical power by dichotomizing data and because individual patient responses may vary over time. (5) Patient global assessments is a generic PRO that assesses if an individual feels better, worse, or unchanged in response to treatment. Although it is widely used in clinical trials and it captures the overall disease impact, it is not heart failure specific and therefore may not capture HRQOL changes targeted by an investigational heart failure therapy.

Patient function can be measured in a variety of ways, including by daily movement metrics, structured and timed submaximal metrics such as the 2-minute walk test or 6-minute walk test (6MWT), structured maximal exertion evaluations such as cardiopulmonary exercise testing, and other aggregations such as the Short Physical Performance Battery, which comprises evaluations of standing balance, 4-meter walk time, and time to complete 5 chair stands. The 6MWT is most suitable to measure the effects of interventions with mechanisms of action that improve functional capacity. Clinically meaningful difference in 6MWT distance has been reported to be thirty meters but alternative values, including a 10% change, may be more appropriate and merit further investigation. (11, 12)

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.

Systematic Reviews

In 2020, Cai et al. published a meta-analysis evaluating the efficacy of baroreflex activation therapy for heart failure. (13) The meta-analysis included 4 RCTs and concluded that baroreflex activation therapy significantly improves quality of life score, 6-minute hall walk distance, New York Heart Association (NYHA) class, N-terminal pro-B-type natriuretic peptide (NT-proBNP), and duration of hospitalization compared to control. However, the 4 RCTs included in the analysis all represented the same patient population from the Hope for Heart Failure (HOPE4HF) study (NCT01471860 and NCT01720160), and did not account for the overlapping population between studies. Therefore, this meta-analysis likely overestimated the true effect of baroreflex activation therapy. The HOPE4HF RCT and post hoc/subgroup analyses are summarized below.

Coats et al. (2022) conducted a patient-level meta-analysis (N=554) comparing patients who received baroreceptor activation therapy in addition to guideline-directed medical therapy or guideline-directed medical therapy alone. (14) Patients included in the analysis were enrolled in 1 of 2 RCTs (HOPE4HF and Barostim Neo-Baroreflex Activation Therapy for Heart Failure [BeAT-HF; both described below]). The studies were conducted between 2012 and 2018 in North American and European countries and enrolled patients with a left ventricular ejection fraction (LVEF) less than or equal to 35%. More than 80% of patients were male and all had NYHA Class III heart failure (or Class II with a recent history of Class III). Similar to the results of the individual trials, at 6 months, patients treated with baroreceptor activation therapy had improved 6-minute hall walk distance (48.5 meters; 95% confidence interval [CI], 32.7 to 64.2). More patients had improvements in NYHA in the baroreceptor activation therapy group with 3.4 higher odds of improving at least 1 NYHA class compared to medical therapy alone. Quality of life as measured by the Minnesota Living with Heart Failure Questionnaire (MLHFQ) was also improved with the addition of baroreceptor activation therapy (-13.4 points; 95% CI, -17.1 to -9.6). This analysis is limited by the small number of RCTs and the open-label design of these trials.

Randomized Controlled Trials

In 2019, the Barostim Neo System was the first device to receive premarket approval through the U.S. Food and Drug Administration's (FDA's) Expedited Access Pathway (see Regulatory section). (2) The safety and effectiveness data reviewed by the FDA was reported in the BeAT-HF trial. (3, 15)

BeAT-HF examined the safety and effectiveness of baroreflex activation therapy in patients with heart failure with reduced ejection fraction using an Expedited and Extended Phase design. In the Expedited Phase, baroreflex activation therapy plus guideline-directed medical therapy was compared at 6 months post-implant to guideline-directed medical therapy alone using 3 intermediate end points: 6-minute hall walk distance, MLHFQ, and NT-proBNP. (15) The rate of heart failure morbidity and cardiovascular mortality was compared between the arms to evaluate early trending using predictive probability modeling.

In the Expedited Phase, investigators randomized 264 intended use patients (White, 73%; Black, 17%; Asian, 1.9%). (15) The primary safety endpoint was major adverse neurological and cardiovascular event free rate, which was only measured in the baroreflex group; the lower bound of the one-sided 95% CI of the event-free rate had to be greater than 85%. Results analysts were blinded to arm assignment. At 6 months, the major adverse neurological and cardiovascular event-free rate was 96.8% (121 of 125 patients), and the one-sided 95% CI lower bound was 92.8% (p<.001). Effectiveness endpoint results are summarized in Table 1. The FDA concluded from these results that the system was safe for the intended use population, and all effectiveness endpoints showed a statistically significant benefit for baroreflex activation therapy plus guideline-directed medical therapy compared to guideline-directed medical therapy alone. In the Expedited Phase, baroreflex activation therapy plus guideline-directed medical therapy was compared at 6 months post-implant to guideline-directed medical therapy alone using 3 intermediate end points: 6-minute hall walk distance, MLHFQ, and NT-proBNP end point is based on an expected event rate of 0.4 events/patient/year in the guideline-directed medical therapy arm.

Table 1. 6-Month Change from Baseline for Effectiveness Endpoints in the BeAT-HF Expedited Phase Trial

	6MHWD		**QOL[a]**		**NT-proBNP**	
	BAT + GDMT	**GDMT**	**BAT + GDMT**	**GDMT**	**BAT + GDMT**	**GDMT**
n	118	120	120	125	120	123
Mean (SD)	48.6 (66.3)	-7.9 (88.4)	-20.7 (25.4)	-6.2 (20.1)	-21.1% (0.4)	3.3% (0.3)
95% CI	36.5 to 60.7	-23.9 to 8.1	-25.3 to -16.1	-9.8 to -2.7	-32.3% to -8.2%	-8.9% to 17.2%
Difference	60.1		-14.1		-24.6%	
95% CI	40.3 to 79.9		-19.2 to -8.9		-37.6% to -8.7%	
p-value	<0.001		<0.001		.004	

6MHWD: 6-minute hall walk distance; BAT: Barostim therapy; BeAT-HF: Barostim Neo-Baroreflex Activation Therapy for Heart Failure; CI: confidence interval; GDMT: guideline-directed medical therapy; NT-proBNP: N-terminal pro-B-type natriuretic peptide; QOL: quality of life; SD: standard deviation.
[a] Measured by the Minnesota Living With Heart Failure Quality of Life questionnaire.

The BeAT-HF Extended phase study enrolled 323 patients with New York Heart Association (NYHA) class III heart failure with reduced ejection fraction (White, 73%; Black, 16.4%; Asian, 1.5%). (16) The trial included 264 patients in the expedited phase and an additional 59 patients who were randomized from May 2019 to June 2020. The study population had an ejection fraction ≤35%, a recent heart failure hospitalization or elevated NT-proBNP levels, and no indication for cardiac resynchronization therapy. Participants were randomized to receive either BAT plus optimal medical management (n=163) or optimal medical management alone (n=163) and were followed for a median of 3.6 years post-intervention. The primary outcome was a composite of cardiovascular mortality (i.e., sudden death, heart failure, myocardial infarction, cerebrovascular accident, cardiovascular procedure, other cardiac death, other vascular death, or death of an unknown cause) and heart failure morbidity (i.e., worsening HF events that led to a hospitalization or ER visit for worsening HF, implantation of a cardiac assist device or heart transplantation). Secondary outcomes assessed the durability of safety, patient-centered symptomatic improvement (quality of life, exercise capacity, and functional status), a hierarchical composite win ratio, freedom from all-cause death left ventricular assist device (LVAD) implantation, and heart transplantation. Effectiveness endpoint results are summarized in Table 2. No differences between BAT + GDMT and GMDT alone were observed for the primary composite outcome or its component parts. For exploratory secondary outcomes, BAT was favored over the control group on the 6MHWD, Minnesota Living with Heart Failure Questionnaire, and improvements of 1 or more NYHA classes, but not NT-proBNP or for freedom from all-cause death. Hierarchical composite win ratio (combining cardiovascular mortality, LVAD/heart transplantation, HF event, Unscheduled clinic visits with IV diuretic, change in MLWHF at 12 months ≥ 5 points) favored BAT + GDMT over control for 53.1% of comparisons (Win ratio, 1.26; 95% CI, 1.02 to 1.58; p=.04). The primary safety endpoint, MANCE-free survival, met its pre-specified performance goal of ≥ 85% (154 [97%], p<.001) in the BAT group. The authors stated that the interpretation of the individual levels of the Win Ratio is challenging, as 2 outcome components had less than 60% of heart failure events and unscheduled clinic visits evaluated. Major limitations of the study included a lack of blinding, the absence of a control group with an implanted device, and changes in care patterns caused by the COVID-19 pandemic, and missing data for some outcomes.

Table 2. Outcomes from the BeAT-HF Extended Phase Trial

Outcome	Time	BAT + GDMT	GDMT	Difference
Primary outcome				
Composite Endpoint	Event Rate per 100 years	32.5	31.5	RR, 0.94 (95% CI, 0.57 to 1.57; p=.82)
CV Mortality	Event Rate (per 100 years)	5	5.9	HR, 0.83 (95% CI, 0.49 to 1.39; p=.47)
HF Morbidity	Event Rate (per 100 years)	27.5	25.6	RR, 0.97 (95% CI, 0.56 to 1.66; p=.90)
Secondary Outcomes				

QoL[a] (Change from BL)	6 months 12 months 24 months	-19.8 -17 -18	-6.3 -8.6 -8	-13.5 (95% CI, -18.1 to -8.9; p<.001) -8.4 (95% CI, -13.1 to -3.7; p<.001) -10 (95% CI, -15.5 to -4.5; p<.001)
6MHWD (Change from BL)	6 months 12 months	46.8 40.6	-8.7 -3	55.5 (95% CI, 37.3 to 73.3; p<.001) 43.5 (95% CI, 25.7 to 61.4; p<.001)
NYHA Class (% of patients improved by ≥ 1 class)	6 months 12 months 24 months	66.6% 72.7% 68%	36.8% 40.8% 41.1%	29.8% (95% CI, 19.1 to 40.5; p<.001) 31.9% (95% CI, 21.2 to 42.5; p<.001) 26.9% (95% CI, 14.4 to 39.4; p<.001)
NT-proBNP	6 months 12 months	-16.7% -8.5%	-0.9% -11%	-17.4 (95% CI, -30.2 to -2.3%; NS) 2.9% (95% CI, -15.4% to 25%; NS)
Win-ratio for hierarchical composite endpoint				Win ratio, 1.26 (95% CI, 1.02 to 1.58; p=.04)
Freedom from all-cause death, LVAD implantation, and heart transplant	Event Rate (per 100 years)	7	10.4	HR, 0.66 (95% CI, 0.43 to 1.01; p=.054)

6MHWD: 6-minute hall walk distance; BAT: Barostim therapy; BeAT-HF: Barostim Neo-Baroreflex Activation Therapy for Heart Failure; CI: confidence interval; CV: cardiovascular; GDMT: guideline directed medical therapy ; HF: heart failure; HR, hazard ratio; NT-proBNP: N-terminal pro-B-type natriuretic peptide; LVAD: left ventricular assist device; NS: not statistically significant; NYHA: New York Heart Association; QOL: quality of life; RR: relative risk; SD: standard deviation.
[a] Measured by the Minnesota Living With Heart Failure Quality of Life questionnaire.

Abraham et al. (2015) reported on the HOPE4HF RCT that evaluated baroreflex stimulation for the treatment of heart failure. This trial was nonblinded and included 146 patients (White, 81.7% and 89.9% in treatment and control groups, respectively) with NYHA Class III heart failure and an ejection fraction of less than or equal to 35% despite guideline-directed medical therapy. (17) Patients were randomized to baroreflex stimulation (Barostim Neo System) plus medical therapy (n=76) or to continued medical therapy alone (n=70) for 6 months. The primary safety outcome was the proportion of patients free from major adverse neurologic and

cardiovascular events. The trialists specified 3 primary efficacy endpoints: changes in NYHA functional class, quality of life score, and 6-minute walk distance.

The overall major adverse neurologic and cardiovascular events-free rate was 97.2%; rates were not reported separately for the baroreflex stimulation and control groups. (17) In terms of the efficacy outcomes, there was significant improvement in the baroreflex stimulation group versus the control group on each of the 3 outcomes. Significantly more patients in the treatment group (55%) improved by at least 1 level in NYHA functional class than in the control group (24%; p<.002). Mean quality of life scores, as assessed by the MLHFQ , improved significantly more in the treatment group (–17.4 points) than in the control group (2.1 points; p<.001). Similarly, mean 6-minute walk distance improved significantly more in the treatment group (59.6 meters) than in the control group (1.5 meters; p=.004).

Weaver et al. (2016) reported 12-month results for 101 (69%) of 146 patients from this RCT. (18) No additional system- or procedure-related major adverse neurologic and cardiovascular events occurred between 6 and 12 months. Moreover, outcomes for NYHA functional class improvement, quality of life score, and 6-minute walk distance were all significantly better in the treatment group than in the control group at 12 months. This analysis had a substantial amount of missing data.

Halbach et al. (2018) published a post hoc subgroup analysis from HOPE4HF evaluating baroreflex activation treatment for heart failure in patients with and without coronary artery disease (CAD). (19) Patients (N=146) from 45 centers with LVEF less than 35% and NYHA Class III were randomized to the baroreflex activation treatment group (n=76) or control group (n=70). The rate of system- or procedure-related major adverse neurological or cardiovascular events was 3.8% for the CAD group and 0% for the no-CAD group (p>.99), while the system- or procedure-related complication rate was 11.5% for patients with CAD and 21.1% for those without CAD (p=.44). In the baroreflex activation group, from baseline to 6 months, quality of life scores decreased by 16.8 ± 3.4 points for CAD patients and by 18.9 ± 5.3 for no-CAD patients; NYHA classification decreased by 0.6 ± 0.1 for CAD patients and by 0.4 ± 0.2 for no-CAD patients. Left ventricular ejection fraction increased by 1.2 ± 1.4 for the CAD group and 5.2 ± 1.9 for the no-CAD group. No interaction was found between the presence of CAD and effect of baroreflex activation therapy (p>.05). The study was limited by its small sample size and by the subgroup analysis not being prespecified.

Overall, the limitations of this RCT included a relatively small sample size for a common condition, relatively short intervention period, and lack of blinding; some of the positive findings on the subjective patient-reported outcomes might have been due at least in part to a placebo effect. Additional RCTs with larger sample sizes and longer follow-up are needed to confirm these positive findings.

Non-Randomized Controlled Trials

Guckel et al. (2023) conducted a single-center prospective study evaluating BAT in 40 consecutive heart failure with reduced ejection fraction patients (mean age, 71 years; 20%

female) with an indication for BAT. (20) The study aimed to analyze patients' acceptance of BAT and outcomes compared to patients treated with GDMT, as well as the effects of angiotensin-receptor neprilysin inhibitors (ARNIs) on BAT response. Ten patients (25%) opted for BAT implantation, and the remaining 30 patients served as the control group. At 12 months follow-up BAT patients showed significant improvements in LVEF (+10% vs. +3%; p=.005), NYHA class ≥ 3 (88% improvement vs. -9%; p=.014), QoL on the EQ-5D-5L (+21% vs 0%; p=.020), NT-proBNP levels (-24% vs 35%; p=.044) and lower heart failure hospitalization rates compared to the control group (50% vs. 83%, p =.020). A subgroup analysis of these outcomes showed that patients who were treated with ARNIs in addition to BAT had greater effects than ARNIs alone. Major limitations of the trial include an absence of power calculations, a small sample size, and imbalances in patient characteristics.

Section Summary: Treatment Resistant Heart Failure

The available evidence for baroreflex activation therapy for heart failure includes 2 RCTs, a post hoc subgroup analysis of an RCT, a non-randomized controlled trial, and meta-analyses of these RCTs. Both RCTs compared baroreflex stimulation plus medical therapy with medical therapy alone in patients with heart failure. The expedited trial phase was used by the FDA to approve the Barostim Neo System and demonstrate that the system is safe and effective for its intended use population. In the expedited phase, baroreflex stimulation significantly improved the primary outcomes of QoL, 6MHWD, and NT-proBNP compared to the control group. However, the trial failed to meet its primary efficacy composite outcome of cardiovascular mortality and heart failure morbidity in the extended phase of the trial but met the pre-specified safety outcome. Secondary outcomes in the extended phase, including QoL, NYHA class, and 6MHWD, showed a significant advantage for the baroreflex stimulation plus medical therapy group for up to 24 months post-intervention, these improvements exceeded the identified minimally important clinical differences for QoL and 6MHWD. A 2018 RCT found a low rate of major adverse events and met all 3 efficacy endpoints (improvements in NYHA functional class, quality of life, and 6-minute walk distance). However, the study had methodologic limitations, including lack of blinding, a relatively small sample size for a common condition, and relatively short intervention period. The non-randomized study found that baroreflex stimulation was associated with improvements in LVEF, NYHA class, QoL, and NT-proBNP levels relative to guide-line directed medical therapy at 12 months post-intervention.

Summary of Evidence

For individuals who have treatment-resistant heart failure who receive baroreflex stimulation therapy, the evidence includes 2 RCTs, a post hoc subgroup analysis of an RCT, a non-randomized controlled trial, and meta-analyses of these trials. Relevant outcomes are OS, functional outcomes, quality of life, hospitalizations, medication use, and treatment-resistant morbidity. The expedited phase of a 2019 RCT was used by the U.S. Food and Drug Administration to approve the Barostim Neo System. The trial demonstrated that the system is safe and met its primary efficacy endpoints of improving quality of life (QoL), 6 minute hall walking distance (6MHWD), and NT-proBNP levels in the short term. In the extended phase of the trial, no statistically significant benefit for the primary efficacy composite outcome of cardiovascular mortality and heart failure morbidity was observed. The pre-specified safety

outcome and secondary outcomes in the extended phase were met. QoL, NYHA class, and 6MHWD showed a statistically and clinically significant advantage for the baroreflex stimulation plus medical therapy group through up to 2 years post-treatment. A 2018 RCT met all 3 efficacy endpoints but had methodologic limitations, incomplete blinding, a relatively small sample size for a common condition, and a short intervention period. The non-randomized study found that baroreflex stimulation was associated with improvements in left ventricular ejection fraction (LVEF), New York Heart Association (NYHA) class, QoL, and NT-proBNP levels relative to guideline-directed medical therapy (GDMT) at 12 months post-intervention. Overall, baroreflex stimulation demonstrates a favorable safety profile and produces modest improvements in functional capacity and quality of life; however, it has not shown significant reductions in either heart failure morbidity or mortality compared to guideline-directed medical therapy. Existing trials suffer from methodological limitations, highlighting the need for a rigorously designed sham-controlled study. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Practice Guidelines and Position Statements

American Heart Association et al.

In 2022, the American Heart Association, American College of Cardiology, and multiple other organizations published a guideline on management of heart failure. (21) The guideline states that baroreceptor stimulation has produced mixed results, and data regarding mortality and hospitalization are lacking.

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this policy are listed in Table 3.

Table 3. Summary of Key Ongoing and Unpublished Trials

NCT Number	Trial Name	Planned Enrollment	Completion Date
NCT01679132[a]	CVRx Barostim Hypertension Pivotal Trial	10	Mar 2026 (suspended; company resources only allows adequate oversight for 1 pivotal trial at a time); last update posted Dec 2021
NCT04502316[a]	Real-World Experience -- Barostim™ Advancing the Level of Clinical Evidence (REBALANCE Registry) A Post-Market Registry With the Barostim™ System	5000	Jun 2028
NCT02876042[a]	BAROSTIM THERAPY ™ in Heart Failure With Preserved Ejection Fraction: A Post-Market Registry	70	Jul 2024 (unknown status)

	With the CE-Marked BAROSTIM NEO™ System		
NCT02880618[a]	BAROSTIM THERAPY™ in Heart Failure With Reduced Ejection Fraction: A Post-Market Registry With the CE-Marked BAROSTIM NEO™ System	500	Jul 2024 (unknown status)
NCT02880631[a]	BAROSTIM THERAPY™ In Resistant Hypertension: A Post-Market Registry With the CE-Marked BAROSTIM NEO™ System	500	Jul 2024 (unknown status)
NCT01471834[a]	Neo Non-Randomized Hypertension Study	40	Aug 2026

NCT: national clinical trial.

[a] Denotes industry-sponsored or cosponsored trial.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	64654, 64655, 64656, 64657, 64658, 64659, 93145, 93146, [Deleted 1/1/2026: 0266T, 0267T, 0268T, 0269T, 0270T, 0271T, 0272T, 0273T]
HCPCS Codes	C1825

*Current Procedural Terminology (CPT®) ©2024 American Medical Association: Chicago, IL.

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Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision

Date	Description of Change
10/15/2025	Document updated with literature review. The following change was made to Coverage: Language related to baroreflex stimulation therapy for individuals with treatment-resistant hypertension was removed, as the device is no longer marketed for this indication; the remaining coverage statement was slightly changed without change to intent. Added references 4-12, 16, and 20; others removed.
04/01/2025	Document updated with literature review. Coverage unchanged. No new references added.
10/15/2024	Reviewed. No changes.
01/01/2024	Document updated with literature review. Coverage unchanged. Added references 11 and 13.
09/15/2022	Document updated with literature review. Coverage unchanged. Added references 10, 11, 15, and 16.
08/01/2021	Reviewed. No changes.
09/01/2020	Document updated with literature review. Coverage unchanged. Added references 2, 3, and 10.
08/01/2019	Reviewed. No changes.

10/15/2018	Document updated with literature review. The following change was made to Coverage: 1) modified examples of experimental, investigational and/or unproven indications to include heart failure. Added references: 1-2, 8, 10-11.
08/15/2017	Reviewed. No changes.
08/15/2016	Document updated with literature review. Coverage unchanged.
10/01/2015	Reviewed. No changes.
06/15/2014	Document updated with literature review. Coverage revised to note that the use of baroreflex stimulation devices is considered experimental, investigational and/or unproven for all indications including but not limited to: related conditions associated with high sympathetic tone. Title changed from: Baroreflex Activation Therapy (BAT) for the Treatment of Drug-Resistant Hypertension.
07/01/2011	New medical document. Baroreflex Activation Therapy (BAT) ® for the treatment of drug-resistant hypertension, using any carotid sinus stimulation device (e.g., Rheos Baroreflex Hypertension Therapy System®), is considered experimental, investigational and unproven.