Radiofrequency Ablation of the Renal Sympathetic Nerves as a Treatment for Uncontrolled Hypertension

Policy # 00465
Original Effective Date: 08/19/2015
Current Effective Date: 05/13/2024

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Note: Baroreflex Stimulation Devices is addressed separately in medical policy 00315.

Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers radiofrequency ablation (RFA) of the renal sympathetic nerves for the treatment of uncontrolled hypertension to be **investigational.***

Background/Overview

Uncontrolled Hypertension

Hypertension is estimated to affect approximately 30% of the population in the U.S. It accounts for a high burden of morbidity related to stroke, ischemic heart disease, kidney disease, and peripheral arterial disease. An estimated 1 in 4 adults with hypertension have their hypertension under control, but the remaining 77% (93 million) remain uncontrolled. Uncontrolled hypertension is diagnosed when an individual's blood pressure remains above targeted levels when a patient either is not using, or unable to use, treatments to control blood pressure or when hypertension persists despite antihypertensive therapies. The definition of uncontrolled hypertension is inclusive of resistant hypertension in which blood pressure remains above the targeted range despite the use of 3 or more antihyperensive medications, including a diuretic, with complementary mechanisms of action. A number of factors may contribute to uncontrolled hypertension including nonadherence to medications, excessive salt intake, inadequate doses of medications, excess alcohol intake, volume overload, drug-induced hypertension, and other forms of secondary hypertension. Also, sometimes it is necessary to address comorbid conditions (ie, obstructive sleep apnea) to control blood pressure adequately.

Treatment

Radiofrequency Denervation of the Renal Sympathetic Nerves
Increased sympathetic nervous system activity has been linked to essential hypertension. Surgical sympathectomy has been shown to be effective in reducing blood pressure but is limited by the adverse events of surgery and was largely abandoned after effective medications for hypertension became available. The renal sympathetic nerves arise from the thoracic nerve roots and innervate the renal artery, the renal pelvis, and the renal parenchyma. Radiofrequency ablation (RFA) is thought to decrease both the afferent sympathetic signals from the kidney to the brain and the efferent signals from the brain to the kidney. This procedure decreases sympathetic activation, decreases vasoconstriction, and decreases activation of the renin-angiotensin system.

The procedure is performed percutaneously with access at the femoral artery. A flexible catheter is threaded into the renal artery, and a controlled energy source, most commonly low-power RF energy, is delivered to the arterial walls where the renal sympathetic nerves are located. Once adequate RF energy has been delivered to ablate the sympathetic nerves, the catheter is removed.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
No RFA devices have been approved by the U.S. Food and Drug Administration (FDA) for ablation of the renal sympathetic nerves as a treatment for hypertension. Several devices have been developed for this purpose and are in various stages of application for FDA approval (FDA product code: DQY):

- The Symplicity Spyral™‡ Renal Denervation System (Medtronic) is a multielectrode RFA catheter system designed to deliver 4-quadrant ablations. On August 23, 2023 the FDA Advisory Committee for Circulatory System Devices voted that the Symplicity Spyral system met its safety endpoint as well as its efficacy endpoint, but after a tied vote in which the chairperson cast the final vote, the committee determined that the device did not achieve a positive balance of benefits and harms.
- The EnligHTN™‡ Multi-Electrode Renal Denervation System (St. Jude Medical) is an RFA catheter using a 4-point multiablation basket design. In January 2014, the EnligHTN™‡ Renal Guiding Catheter was cleared for marketing by the FDA through the 510(k) process, based

on substantial equivalence to predicate devices for the following indication: percutaneous use through an introducer sheath to facilitate a pathway to introduce interventional and diagnostic devices into the renal arterial vasculature.

- The Vessix™‡ Renal Denervation System (Boston Scientific; formerly the V2 renal denervation system, Vessix Vascular) is a combination of an RF balloon catheter and bipolar RF generator technologies, intended to permit a lower voltage intervention.

Other RFA catheters (eg, Thermocouple Catheter™‡ [Biosense Webster]) used for other types of ablation procedures (eg, cardiac electrophysiology procedures) have been used off-label for RFA of the renal arteries.

In 2020, the FDA granted breakthrough therapy designation to 2 renal artery denervation systems - SoniVie's Therapeutic Intra-Vascular Ultrasound (TIVUS) System and Recor's Paradise Renal Denervation System - for the treatment of patients with persistently elevated blood pressure. However, ultrasound-based renal denervation systems are outside of the scope of this medical policy.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Description

Radiofrequency ablation (RFA) of the renal sympathetic nerves is thought to decrease both the afferent sympathetic signals from the kidney to the brain and the efferent signals from the brain to the kidney. This procedure decreases sympathetic activation, decreases vasoconstriction, and decreases activation of the renin-angiotensin system. Radiofrequency ablation of the renal sympathetic nerves may act as a nonpharmacologic treatment for hypertension and has been proposed as a treatment option for patients with uncontrolled hypertension despite the use of anti-hypertensive medications.

Summary of Evidence
For individuals who have uncontrolled hypertension, despite the use of anti-hypertensive medications, who receive RFA of the renal sympathetic nerves, the evidence includes several RCTs, numerous systematic reviews of the RCTs, and a multinational registry study. Relevant outcomes are symptoms, change in disease status, morbid events, medication use, and treatment-related morbidity. The proof of principle SPYRAL HTN-OFF MED study found that multielectrode renal denervation was superior to sham in the absence of background antihypertensive medication therapy, with between-group differences of -4.0 mmHg for 24-h SBP and -6.6 for office SBP at 3 months. The unpowered SPYRAL HTN-ON MED Pilot study also found significant between-group differences of -7.4 mmHg for 24-h SBP and -6.8 mmHg for office SBP at 6 months; however, results were only significant for the subgroup of patients non-adherent to medications. Long-term data from the SPYRAL HTN-ON MED study suggest that blood pressure reductions with multielectrode renal denervation are progressive and sustained over time. The SPYRAL HTN-ON MED Expansion study failed to meet its primary efficacy endpoint and found only 0.03 mmHg difference between renal denervation and sham control groups at 6 months follow-up. A significant reduction in office blood pressure was noted at 6 months (-4.1 mmHg). Confounding of these outcome estimates by unbalanced medication changes, missing 24-h SBP outcome data, and timing of antihypertensive medications related to 24-h SBP assessment may explain the discordant results between the pilot and expansion phases of this trial. Study interpretation is also complicated by short-term blinded follow-up and imputation of excluded crossover patient data. It is unclear which patients are most likely to derive benefit, and currently, there is no practical method to verify nerve destruction following ablation. Evidence from systematic reviews and meta-analyses are conflicting, but all available studies included evidence from both first and second-generation Symplicity catheters as well as multiple renal denervation methodologies such as ultrasound. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Supplemental Information

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.

American Heart Association et al
The American Heart Association (AHA), American College of Cardiology (AHA), and American Society of Hypertension (ASH; 2015) issued joint guidelines on the treatment of hypertension in patients with coronary artery disease. The guidelines noted the Symplicity HTN-3 trial did not find a significant benefit from renal denervation and stated that additional randomized controlled trials would be needed.

The AHA, ACC, and 9 additional specialty societies (2018) published joint guidelines on the prevention, detection, evaluation, and management of high blood pressure in adults. In discussing resistant hypertension, the guidelines indicated that studies using catheter ablation of renal sympathetic nerves "have not provided sufficient evidence to recommend the use of these devices."

The AHA (2018) published a Scientific Statement on the detection, evaluation, and management of resistant hypertension. The AHA Statement discussed the lack of benefit found in the Symplicity HTN-3 trial, as well as its methodological limitations. The statement also referred to the more recent positive data from the SPYRAL HTN-OFF MED trial, but noted that because the enrolled patients did not have resistant hypertension, "at best, this represents a proof-of-principle study demonstrating the role of the renal sympathetic nervous system in hypertension." The statement concluded that "the role of device-based sympatholytic treatments, as with renal denervation and baroreceptor stimulation, awaits clarification."

Eighth Joint National Committee
The Eighth Joint National Committee (2014), which was appointed to provide recommendations on hypertension treatment, published an evidence-based guideline on the management of hypertension in adults. These recommendations did not discuss the use of renal denervation.

European Society for Hypertension (ESH)
The ESH, with endorsement by the European Renal Association and the International Society of Hypertension, issued guidance on the management of arterial hypertension in 2023. The following recommendations were issued concerning renal denervation:

- Renal denervation can be considered as a treatment option in patients with an eGFR of > 40 ml/min/1.73m^2 who have uncontrolled blood pressure despite the use of anti-hypertensive drug combination therapy or if drug treatment elicits serious side effects. (Class of Recommendation: II, Level of Evidence: B)
- Renal denervation can be considered as an additional treatment option in patients with resistant hypertension if eGFR is > 40 ml/min/1.73m^2. (Class of Recommendation: II, Level of Evidence: B)
- Selection of patients to whom renal denervation is offered should be done in a shared decision-making process after objective and complete patient information is collected. (Class of Recommendation: I, Level of Evidence: C)
- Renal denervation should only be performed in experienced specialized centers to guarantee appropriate selection of eligible patients and completeness of the denervation procedure. (Class of Recommendation: I, Level of Evidence: C)

A class of recommendation I indicates a general consensus that the measure is useful, and a class II recommendation reflects that there is no general consensus and that only doubtful evidence exists. An 'A' level of evidence indicates that RCTs or meta-analyses with cardiovascular disease outcomes are available for this recommendation, a level 'B' suggests RCTs with surrogate measures, observational studies with cardiovascular disease outcomes or meta-analyses are available, and a C recommendation reflects either expert opinion or only observational or lower quality experimental evidence.

ESH recommendations did not discuss the specific use of radiofrequency renal denervation and included evidence from other modalities, such as ultrasound, in their evidence appraisal.

National Institute for Health and Care Excellence
In 2023, the National Institute for Health and Care Excellence (NICE) published an interventional procedures guidance on the use of percutaneous transluminal radiofrequency sympathetic denervation of the renal artery for resistant hypertension, recommending that the procedure should only be used with special arrangements for clinical governance, consent, and audit or research due to limited evidence.

Radiofrequency Ablation of the Renal Sympathetic Nerves as a Treatment for Uncontrolled Hypertension

Policy # 00465
Original Effective Date: 08/19/2015
Current Effective Date: 05/13/2024

U.S. Preventive Services Task Force Recommendations
Not applicable.

Medicare National Coverage
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials
Some currently ongoing and unpublished trials that might influence this review are listed in Table 1.

Table 1. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT02439749[a]	Global Clinical Study of Renal Denervation With the Symplicity Spyral™‡ Multi-electrode Renal Denervation System in Patients With Uncontrolled Hypertension in the Absence of Antihypertensive Medications (SPYRAL HTN-OFF MED)	366	Dec 2023 (ongoing)
NCT04307836[a]	A Prospective, Multicenter, No-treatment Controlled, Randomized, Open-label, Pivotal Study to Evaluate the Safety and Efficacy of DENEX, Renal Denervation Therapy, in Patients with Hypertension on no or 1-3 Antihypertensive Medications	140	Jan 2024 (recruiting)
NCT04535050[a]	A Prospective, Multicenter, Sham-controlled, Single-blinded, Randomized, Pilot Study to Evaluate the Safety and Effectiveness of DENEX Renal Denervation System in Patients With Uncontrolled	100	Mar 2026 (not yet recruiting)

NCT No.	Trial Name	Planned Enrollment	Completion Date
	Hypertension Not Treated With Antihypertensive Medication		
NCT02439775[a]	Global Clinical Study of Renal Denervation With the Symplicity Spyral™‡ Multi-electrode Renal Denervation System in Patients With Uncontrolled Hypertension on Standard Medical Therapy (SPYRAL HTN-ON MED)	337	Jul 2026 (ongoing)
NCT05198674[a]	The SPYRAL AFFIRM Global Clinical Study of Renal Denervation With the Symplicity Spyral Renal Denervation System in Subjects With Uncontrolled Hypertension (SPYRAL AFFIRM)	1200	Jun 2027 (recruiting)
NCT05563337	Renal Denervation in Hypertensive Women Planning to Become Pregnant (WHY-RDN)	80	Aug 2027 (not yet recruiting)
NCT01534299[a]	Global SYMPLICITY Registry (GSR) Denervation Findings in Real World (DEFINE)	5000	Oct 2027 (recruiting)
Unpublished			
NCT04311086[a]	Global Clinical Study of Renal Denervation in the Distal Main and First Order Branch Renal Arteries Using the Symplicity Spyral™‡ Multi-electrode Renal Denervation System (SPYRAL DYSTAL)	56	Jan 2023 (completed)
NCT04722159	Clinical Outcome of Patients With Resistant Hypertension Undergoing Renal Denervation: A Report From the Swedish Registry for Renal Denervation	300	Aug 2021 (unknown)

NCT: national clinical trial.
[a] Denotes industry-sponsored or cosponsored trial.

References

1. Acelajado MC, Calhoun DA. Resistant hypertension, secondary hypertension, and hypertensive crises: diagnostic evaluation and treatment. Cardiol Clin. Nov 2010; 28(4): 639-54. PMID 20937447
2. Centers for Disease Control and Prevention (CDC). Facts About Hypertension, Updated July 6, 2023; https://www.cdc.gov/bloodpressure/facts.htm.
3. Food and Drug Administration (FDA) Circulatory System Devices Panel. FDA Executive Summary, Premarket Application (PMA) for Pxxxxxx Medtronic, Inc. Symplicity Spyral Renal Denervation System. 2023; https://www.fda.gov/media/171411/download.
4. Doumas M, Papademetriou V, Douma S, et al. Benefits from treatment and control of patients with resistant hypertension. Int J Hypertens. Dec 22 2010; 2011: 318549. PMID 21234402
5. Zile MR, Little WC. Effects of autonomic modulation: more than just blood pressure. J Am Coll Cardiol. Mar 06 2012; 59(10): 910-2. PMID 22381426
6. Townsend RR, Mahfoud F, Kandzari DE, et al. Catheter-based renal denervation in patients with uncontrolled hypertension in the absence of antihypertensive medications (SPYRAL HTN-OFF MED): a randomised, sham-controlled, proof-of-concept trial. Lancet. Nov 11 2017; 390(10108): 2160-2170. PMID 28859944
7. Böhm M, Kario K, Kandzari DE, et al. Efficacy of catheter-based renal denervation in the absence of antihypertensive medications (SPYRAL HTN-OFF MED Pivotal): a multicentre, randomised, sham-controlled trial. Lancet. May 02 2020; 395(10234): 1444-1451. PMID 32234534
8. Kandzari DE, Böhm M, Mahfoud F, et al. Effect of renal denervation on blood pressure in the presence of antihypertensive drugs: 6-month efficacy and safety results from the SPYRAL HTN-ON MED proof-of-concept randomised trial. Lancet. Jun 09 2018; 391(10137): 2346-2355. PMID 29803589
9. Mahfoud F, Kandzari DE, Kario K, et al. Long-term efficacy and safety of renal denervation in the presence of antihypertensive drugs (SPYRAL HTN-ON MED): a randomised, sham-controlled trial. Lancet. Apr 09 2022; 399(10333): 1401-1410. PMID 35390320

10. Kandzari DE, Kario K, Mahfoud F, et al. The SPYRAL HTN Global Clinical Trial Program: Rationale and design for studies of renal denervation in the absence (SPYRAL HTN OFF-MED) and presence (SPYRAL HTN ON-MED) of antihypertensive medications. Am Heart J. Jan 2016; 171(1): 82-91. PMID 26699604
11. Coppolino G, Pisano A, Rivoli L, et al. Renal denervation for resistant hypertension. Cochrane Database Syst Rev. Feb 21 2017; 2(2): CD011499. PMID 28220472
12. Chen XH, Kim S, Zeng XX, et al. Account for Clinical Heterogeneity in Assessment of Catheter-based Renal Denervation among Resistant Hypertension Patients: Subgroup Meta-analysis. Chin Med J (Engl). Jul 05 2017; 130(13): 1586-1594. PMID 28639575
13. Silverwatch J, Marti KE, Phan MT, et al. Renal Denervation for Uncontrolled and Resistant Hypertension: Systematic Review and Network Meta-Analysis of Randomized Trials. J Clin Med. Feb 16 2021; 10(4). PMID 33669195
14. Ogoyama Y, Tada K, Abe M, et al. Effects of renal denervation on blood pressures in patients with hypertension: a systematic review and meta-analysis of randomized sham-controlled trials. Hypertens Res. Feb 2022; 45(2): 210-220. PMID 34657140
15. Pappaccogli M, Covella M, Berra E, et al. Effectiveness of Renal Denervation in Resistant Hypertension: A Meta-Analysis of 11 Controlled Studies. High Blood Press Cardiovasc Prev. Jun 2018; 25(2): 167-176. PMID 29752703
16. Fadl Elmula FEM, Feng YM, Jacobs L, et al. Sham or no sham control: that is the question in trials of renal denervation for resistant hypertension. A systematic meta-analysis. Blood Press. Aug 2017; 26(4): 195-203. PMID 28443356
17. Sun D, Li C, Li M, et al. Renal Denervation vs Pharmacotherapy for Resistant Hypertension: A Meta-Analysis. J Clin Hypertens (Greenwich). Aug 2016; 18(8): 733-40. PMID 26619813
18. Zhang X, Wu N, Yan W, et al. The effects of renal denervation on resistant hypertension patients: a meta-analysis. Blood Press Monit. Aug 2016; 21(4): 206-14. PMID 26901340
19. Yao Y, Zhang D, Qian J, et al. The effect of renal denervation on resistant hypertension: Meta-analysis of randomized controlled clinical trials. Clin Exp Hypertens. 2016; 38(3): 278-86. PMID 27018652
20. Fadl Elmula FE, Jin Y, Yang WY, et al. Meta-analysis of randomized controlled trials of renal denervation in treatment-resistant hypertension. Blood Press. 2015; 24(5): 263-74. PMID 26194721
21. Rosendorff C, Lackland DT, Allison M, et al. Treatment of hypertension in patients with coronary artery disease: a scientific statement from the American Heart Association, American

College of Cardiology, and American Society of Hypertension. Circulation. May 12 2015; 131(19): e435-70. PMID 25829340
22. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension. Jun 2018; 71(6): 1269-1324. PMID 29133354
23. Carey RM, Calhoun DA, Bakris GL, et al. Resistant Hypertension: Detection, Evaluation, and Management: A Scientific Statement From the American Heart Association. Hypertension. Nov 2018; 72(5): e53-e90. PMID 30354828
24. James PA, Oparil S, Carter BL, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). JAMA. Feb 05 2014; 311(5): 507-20. PMID 24352797
25. Mancia G, Kreutz R, Brunström M, et al. 2023 ESH Guidelines for the management of arterial hypertension The Task Force for the management of arterial hypertension of the European Society of Hypertension Endorsed by the International Society of Hypertension (ISH) and the European Renal Association (ERA). J Hypertens. Jun 21 2023. PMID 37345492
26. National Institute for Health and Care Excellence (NICE). Interventional procedures guidance: Percutaneous transluminal radiofrequency sympathetic denervation of the renal artery for resistant hypertension [IPG418]. March 2023; https://www.nice.org.uk/guidance/ipg754.

Policy History

Original Effective Date: 08/19/2015
Current Effective Date: 05/13/2024

08/06/2015	Medical Policy Committee review
08/19/2015	Medical Policy Implementation Committee approval. New Policy
08/04/2016	Medical Policy Committee review
08/17/2016	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/01/2017	Coding update: Removing ICD-9 Diagnosis Codes
11/02/2017	Medical Policy Committee review

Policy # 00465
Original Effective Date: 08/19/2015
Current Effective Date: 05/13/2024

11/15/2017	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
11/08/2018	Medical Policy Committee review
11/21/2018	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
11/07/2019	Medical Policy Committee review
11/13/2019	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
04/02/2020	Medical Policy Committee review
04/08/2020	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
04/01/2021	Medical Policy Committee review
04/14/2021	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
04/07/2022	Medical Policy Committee review
04/13/2022	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
04/06/2023	Medical Policy Committee review
04/12/2023	Medical Policy Implementation Committee approval. Title changed from "Radiofrequency Ablation of the Renal Sympathetic Nerves as a Treatment for Resistant Hypertension" to "Radiofrequency Ablation of the Renal Sympathetic Nerves as a Treatment for Resistant or Uncontrolled Hypertension." Revised investigational statement to include patients with uncontrolled hypertension. Coverage eligibility unchanged.
04/04/2024	Medical Policy Committee review
04/10/2024	Medical Policy Implementation Committee approval. Title changed from "Radiofrequency Ablation of the Renal Sympathetic Nerves as a Treatment for Resistant or Uncontrolled Hypertension" to "Radiofrequency Ablation of the Renal Sympathetic Nerves as a Treatment for Uncontrolled Hypertension". Removed resistant hypertension from the investigational statement.
12/11/2024	Coding update

Next Scheduled Review Date: 04/2025

Radiofrequency Ablation of the Renal Sympathetic Nerves as a Treatment for Uncontrolled Hypertension

Policy # 00465
Original Effective Date: 08/19/2015
Current Effective Date: 05/13/2024

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2023 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines is with Blue Cross and Blue Shield of Louisiana and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	0338T, 0339T
HCPCS	Add code effective 01/01/2025: C1735
ICD-10 Diagnosis	All related diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into

standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.