Priority Health

MEDICAL POLICY
No. 91644-R0

RENAL DENERVATION FOR RESISTANT HYPERTENSION

Effective Date: February 1, 2025 | **Review Dates: 11/24**
Date Of Origin: November 13, 2024 | **Status: New**

I. POLICY/CRITERIA

A. Ablation of the renal sympathetic nerves using radiofrequency or ultrasound is medically necessary for the treatment of resistant hypertension **when ALL the following criteria are met:**

1. The renal denervation (RDN) procedure is done utilizing an FDA approved device; AND
2. The member is 18 years or older; AND
3. The member has been diagnosed with resistant hypertension (SBP ≥140 mmHg OR DBP ≥90 mmHg) that remains uncontrolled despite 3 blood pressure-lowering medications from different classes at maximally tolerated doses, including a thiazide diuretic; AND
4. Documented evidence or attestation of medication compliance from the treating physician, OR documentation that the member is not able to meet this criterion due to medication intolerance or contraindications; AND
5. Hypertension is confirmed by 24-hour ambulatory blood pressure readings; AND
6. Secondary causes of hypertension (e.g. primary aldosteronism, pheochromocytoma, primary kidney disease, Cushing's syndrome, sleep apnea) have been ruled out; AND
7. eGFR > 40 ml/min/1.73m2

B. Radiofrequency or ultrasound ablation of the renal sympathetic nerves is not medically necessary if any of the following conditions are present:

1. Renal artery fibromuscular dysplasia
2. Stented renal artery (< 3 months prior to radiofrequency ablation procedure)
3. Renal artery aneurysm
4. Actively pregnant or breastfeeding
5. Presence of abnormal kidney (or secreting adrenal) tumors

    a. Known iliac/femoral artery stenosis precluding insertion of the catheter
    b. Main artery length of less than 20mm for ultrasound ablation
    c. Active infection within previous 7 days prior to procedure

C. Ablation of the renal sympathetic nerves is a one-time procedure to be done with either radiofrequency or ultrasound. Repeat therapy is not medically necessary.

D. Ablation of the renal sympathetic nerves using alcohol-mediated RDN (e.g., Peregrine System™) is considered experimental/investigational.

II. MEDICAL NECESSITY REVIEW

Prior authorization for certain drug, services, and procedures may or may not be required. In cases where prior authorization is required, providers will submit a request demonstrating that a drug, service, or procedure is medically necessary. For more information, please refer to the Priority Health Provider Manual.

III. APPLICATION TO PRODUCTS

Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.

- **HMO/EPO:** ***This policy applies to insured HMO/EPO plans.***
- **POS:** ***This policy applies to insured POS plans.***
- **PPO:** ***This policy applies to insured PPO plans. Consult individual plan documents as state mandated benefits may apply. If there is a conflict between this policy and a plan document, the provisions of the plan document will govern.***
- **ASO:** ***For self-funded plans, consult individual plan documents. If there is a conflict between this policy and a self-funded plan document, the provisions of the plan document will govern.***
- **INDIVIDUAL:** ***For individual policies, consult the individual insurance policy. If there is a conflict between this medical policy and the individual insurance policy document, the provisions of the individual insurance policy will govern.***
- **MEDICARE:** ***Coverage is determined by the Centers for Medicare and Medicaid Services (CMS); if a coverage determination has not been adopted by CMS, this policy applies.***
- **MEDICAID/HEALTHY MICHIGAN PLAN:** ***For Medicaid/Healthy Michigan Plan members, this policy will apply. Coverage is based on medical necessity criteria being met and the appropriate code(s) from the coding section of this policy being included on the Michigan Medicaid Fee Schedule located at: http://www.michigan.gov/mdch/0,1607,7-132-2945_42542_42543_42546_42551-159815--,00.html. If there is a discrepancy between this policy and the Michigan Medicaid Provider Manual located at: http://www.michigan.gov/mdch/0,1607,7-132-2945_5100-87572--,00.html, the Michigan Medicaid Provider Manual will govern. If there is a discrepancy or lack of guidance in the Michigan Medicaid Provider Manual, the Priority Health contract with Michigan Medicaid will govern. For Medical Supplies/DME/Prosthetics and Orthotics, please refer to the Michigan Medicaid Fee Schedule to verify coverage.***

IV. BACKGROUND

Renal nerves play a critical role in regulating blood pressure and fluid volume, and their dysfunction is closely related with cardiovascular diseases. Renal nerves are composed of sympathetic efferent and sensory afferent nerves. Activation of the efferent renal sympathetic nerves induces renin secretion, sodium absorption, and increased renal vascular resistance, which lead to increased blood pressure and fluid retention. Afferent renal sensory nerves, which are densely innervated in the renal pelvic wall, project to the hypothalamic paraventricular nucleus in the brain to modulate sympathetic outflow to the periphery, including the heart, kidneys, and arterioles. The effects of renal denervation on the cardiovascular system are mediated by both efferent denervation and afferent denervation. (*Katsurada et al., 2021*)

Renal denervation (RDN) is a relatively new approach to treating hypertension that involves a controlled damage to the sympathetic innervation within the renal arteries. There are two main types of RDN: radiofrequency ablation (Medtronic Symplicity Spyral) and ultrasound ablation (ReCor Paradise Ultrasound). A third modality, alcohol-mediated RDN (i.e. the Peregrine System) is currently being studied but has not yet received FDA approval.

Radiofrequency Ablation Renal Denervation

Radiofrequency ablation (RFA) uses a catheter to position electrodes (typically 4 spaced approximately 6mm apart in a spiral sequence) that generate heat using medium-frequency alternating current. The heat generated is well tolerated by the wall of the renal artery, but is toxic to the nerves surrounding the artery that are exposed to the heat energy field. The energy field ranges as far as 7mm from the lumen of the artery. *(Rey-García et al, 2023)*

The SPYRAL HTN-OFF Med trial *(Böhm et al., 2020)* was an international, prospective, single-blinded, sham-controlled trial done at 44 study sites. Hypertensive patients with office systolic blood pressure of 150 mm Hg to less than 180 mm Hg were randomly assigned 1:1 to either a renal denervation or sham procedure. The primary efficacy endpoint was baseline-adjusted change in 24-h systolic blood pressure and the secondary efficacy endpoint was baseline-adjusted change in office systolic blood pressure from baseline to 3 months after the procedure. 331 patients were randomly assigned to either renal denervation (n=166) or a sham procedure (n=165). The primary and secondary efficacy endpoints were met, with posterior probability of superiority more than 0·999 for both. The treatment difference between the two groups for 24-h systolic blood pressure was –3·9 mm Hg (Bayesian 95% credible interval –6·2 to –1·6) and for office systolic blood pressure the difference was –6·5 mm Hg (–9·6 to –3·5). No major device-related or procedural-related safety events occurred up to 3 months.

The SPYRAL HTN-ON Med trial *(Kandzari et al., 2018)* was an international, randomized, single-blind, sham-control, proof-of-concept trial enrolling patients with uncontrolled hypertension (aged 20–80 years) at 25 centers. Eligible patients had an office systolic blood pressure of between 150 mm Hg and 180 mm Hg and a diastolic blood pressure of 90 mm Hg or higher; a 24 h ambulatory systolic blood pressure of between 140 mm Hg and 170 mm Hg at second screening; and were on one to three antihypertensive drugs with stable doses for at least 6 weeks. Patients underwent renal angiography and were randomly assigned to undergo renal denervation or sham control. The primary efficacy endpoint was blood pressure change from baseline based on ambulatory blood pressure measurements assessed at 6 months, as compared between treatment groups. Drug surveillance was used to assess medication adherence. Safety events were assessed through 6 months as per major adverse events. Data from the first 80 patients randomly assigned to renal denervation (n=38) and sham control (n=42) were included in the results. Office and 24 h ambulatory blood pressure decreased significantly from baseline to 6 months in the renal denervation group (mean baseline-adjusted treatment differences in 24 h systolic blood pressure –7·0 mm Hg, 95% CI –12·0 to –2·1; p=0·0059, 24 h diastolic blood pressure –4·3 mm Hg, –7·8 to –0·8; p=0.0174, office systolic blood pressure –6·6 mm Hg, –12·4 to –0·9; p=0·0250, and office diastolic blood pressure –4·2 mm Hg, –7·7 to –0·7; p=0·0190). The change in blood pressure was significantly greater at 6 months in the renal denervation group than the sham-control group for office systolic blood pressure (difference –6·8 mm Hg, 95% CI –12·5 to –1·1; p=0·0205), 24 h systolic blood pressure (difference –7·4 mm Hg, –12·5 to –2·3; p=0·0051), office diastolic blood pressure (difference –3·5 mm Hg, –7·0 to –0·0; p=0·0478), and 24 h diastolic blood pressure (difference –4·1 mm Hg, –7·8 to –0·4; p=0·0292). Evaluation of hourly changes in 24 h systolic blood pressure and diastolic blood pressure showed blood pressure reduction throughout 24 h for the renal denervation group. 3 month blood pressure reductions were not significantly different between groups. Medication adherence was about 60% and varied for individual patients throughout the study. No major adverse events were recorded in either group.

The Global SYMPLICITY Registry is a prospective, open-label registry involving 196 active sites worldwide in hypertensive patients receiving RDN treatment. In 2019, Mahfoud and colleagues published 3-year safety and efficacy data from the registry. Among 2237 patients enrolled and treated with the SYMPLICITY Flex catheter (Medtronic inc), 1742 were eligible for follow-up at 3 years. Baseline office and 24-h ambulatory systolic BP (SBP) were 166 ± 25 and 154 ± 18 mmHg, respectively. SBP reduction after RDN was sustained over 3 years, including decreases in both office (-16.5 ± 28.6 mmHg, $P < 0.001$) and 24-h ambulatory SBP (-8.0 ± 20.0 mmHg; $P < 0.001$). Twenty-one percent of patients had a baseline estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m2. From baseline to 3 years, renal function declined by 7.1 mL/min/1.73 m2 in patients without chronic kidney disease (CKD; eGFR ≥ 60 mL/min/1.73 m2;

baseline eGFR 87 ± 17 mL/min/1.73 m2) and by 3.7 mL/min/1.73 m2 in patients with CKD (eGFR <60 mL/min/1.73 m2; baseline eGFR 47 ± 11 mL/min/1.73 m2). No long-term safety concerns were observed following the RDN procedure.

Ultrasound Renal Denervation

Ultrasound approaches deliver a series of ultrasound-emitting sources (typically 4) that are mounted on a catheter with an inflatable balloon system that allows irrigation of the portion of the catheter in contact with the wall of the renal artery with a solution that maintains a cooler temperature in the lumen than in the perivascular space. *(Rey-García et al, 2023)*

RADIANCE-HTN SOLO was a multicenter, international, single-blind, randomized, sham-controlled trial done at 21 centers in the USA and 18 in Europe. Patients with combined systolic–diastolic hypertension aged 18–75 years were eligible if they had ambulatory blood pressure greater than or equal to 135/85 mm Hg and less than 170/105 mm Hg after a 4-week discontinuation of up to two antihypertensive medications and had suitable renal artery anatomy. Patients were randomized (1:1) to undergo renal denervation with the Paradise system (ReCor Medical, Palo Alto, CA, USA) or a sham procedure consisting of renal angiography only. Patients and outcome assessors were blinded to randomization. The primary effectiveness endpoint was the change in daytime ambulatory systolic blood pressure at 2 months in the intention-to-treat population. Patients were to remain off antihypertensive medications throughout the 2 months of follow-up unless specified blood pressure criteria were exceeded. Major adverse events included all-cause mortality, renal failure, an embolic event with end-organ damage, renal artery or other major vascular complications requiring intervention, or admission to hospital for hypertensive crisis within 30 days and new renal artery stenosis within 6 months. 803 patients were screened for eligibility and 146 were randomized to undergo renal denervation (n=74) or a sham procedure (n=72). The reduction in daytime ambulatory systolic blood pressure was greater with renal denervation (–8·5 mm Hg, SD 9·3) than with the sham procedure (–2·2 mm Hg, SD 10·0; baseline-adjusted difference between groups: –6·3 mm Hg, 95% CI –9·4 to –3·1, p=0·0001). No major adverse events were reported in either group. *(Azizi et al., 2018)*

Rader and colleagues (2022) published results on the three-year outcomes of the treatment arm of the RADIANCE-HTN SOLO trial. Fifty-one of 74 patients (age: 53.9±11 years; 67% men) originally randomised to ultrasound RDN (uRDN) completed the 36-month follow-up. Initial screening office blood pressure (OBP) upon study entry was 145/92±14/10 mmHg on a mean of 1.2 antihypertensive medications (AHM) (range: 0-2.0). Baseline OBP after AHM washout was 154/99±13/8 mmHg. At 36 months, patients were on an average of 1.3 AHM (range: 0-3.0) with 8 patients on no AHM. OBP decreased by 18/11±15/9 mmHg from baseline to 36 months (p<0.001 for both). Overall, OBP control

(<140/90 mmHg) improved from 29.4% at screening to 45.1% at 36 months (p=0.059). For patients uncontrolled at screening (n=36), systolic OBP decreased by 10.8 mmHg (p<0.001) at 36 months on similar AHM (p=0.158).

The RADIANCE II trial was a sham-controlled, randomized clinical trial with patients and outcome assessors blinded to treatment assignment that was conducted at 37 centers in the US and 24 centers in Europe. Patients aged 18 years to 75 years with hypertension (seated office systolic BP [SBP] ≥140 mm Hg and diastolic BP [DBP] ≥90 mm Hg despite taking up to 2 antihypertensive medications) were eligible if they had an ambulatory SBP/DBP of 135/85 mm Hg or greater and an SBP/DBP less than 170/105 mm Hg after a 4-week washout of their medications. Patients with an estimated glomerular filtration rate of 40 mL/min/1.73 m2 or greater and with suitable renal artery anatomy were randomized 2:1 to undergo ultrasound renal denervation or a sham procedure. Patients were instructed to abstain from antihypertensive medications until the 2-month follow-up unless prespecified BP criteria were exceeded and were associated with clinical symptoms. Among 1038 eligible patients, 150 were randomized to ultrasound renal denervation and 74 to a sham procedure (mean age, 55 years [SD, 9.3 years]; 28.6% female; and 16.1% self-identified as Black or African American). The reduction in daytime ambulatory SBP was greater with ultrasound renal denervation (mean, −7.9 mm Hg [SD, 11.6 mm Hg]) vs the sham procedure (mean, −1.8 mm Hg [SD, 9.5 mm Hg]) (baseline-adjusted between-group difference, −6.3 mm Hg [95% CI, −9.3 to −3.2 mm Hg], P < .001), with a consistent effect of ultrasound renal denervation throughout the 24-hour circadian cycle. Among 7 secondary BP outcomes, 6 were significantly improved with ultrasound renal denervation vs the sham procedure. No major adverse events were reported in either group. *(Azizi et al., 2023)*

In a recent meta-analysis by Mufarrih and colleagues (2024), online databases were searched to identify randomized clinical trials comparing efficacy and safety of RDN versus control in patients with uncontrolled hypertension. Subgroup analyses were conducted for sham-controlled trials and studies that used RDN devices that have gained or are currently seeking US Food and Drug Administration approval. Fifteen trials with 2581 patients (RDN, 1723; sham, 858) were included. In patients off antihypertensive medications undergoing RDN, a significant reduction in 24-hour ambulatory (−3.70 [95% CI, −5.41 to −2.00] mmHg), office (−4.76 [95% CI, −7.57 to −1.94] mm Hg), and home (−3.28 [95% CI, −5.96 to −0.61] mm Hg) systolic blood pressures was noted. In patients on antihypertensive medications, a significant reduction was observed in 24-hour ambulatory (−2.23 [95% CI, −3.56 to −0.90] mm Hg), office (−6.39 [95% CI,−11.49 to −1.30]), home (−6.08 [95% CI, −11.54 to −0.61] mm Hg), daytime (−2.62 [95% CI, −4.14 to−1.11]), and nighttime (−2.70 [95% CI, −5.13 to −0.27]) systolic blood pressures, as well as 24-hour ambulatory (−1.16 [95% CI, −1.96 to −0.35]), office (−3.17 [95% CI, −5.54 to −0.80]), and daytime (−1.47 [95% CI, −2.50 to −0.27]) diastolic blood pressures. The authors concluded that

RDN significantly lowers blood pressure in patients with uncontrolled hypertension in patients off and on antihypertensive medications, with a favorable safety profile. The efficacy of RDN was consistent in sham-controlled trials and contemporary trials using US Food and Drug Administration–approved devices.

Guidelines and Position Statements

National Institute of Health and Care Excellence (NICE) - Percutaneous Transluminal Renal Sympathetic Denervation for Resistant Hypertension (2023)

- *"Percutaneous transluminal renal sympathetic denervation for resistant hypertension should only be used with special arrangements for clinical governance, consent, and audit or research" (NICE, 2023)*

European Society of Cardiology (ESC) - 2024 ESC Guidelines for the Management of Elevated Blood Pressure and Hypertension

- *"To reduce BP, and if performed at a medium-to-high volume centre, catheter-based renal denervation may be considered for resistant hypertension patients who have BP that is uncontrolled despite a three BP-lowering drug combination (including a thiazide or thiazide-like diuretic), and who express a preference to undergo renal denervation after a shared risk-benefit discussion and multidisciplinary assessment."*
- *"To reduce BP, and if performed at a medium-to-high volume centre, catheter-based renal denervation may be considered for patients with both increased [cardiovascular disease] risk and uncontrolled hypertension on fewer than three drugs, if they express a preference to undergo renal denervation after a shared risk-benefit discussion and multidisciplinary assessment."*
- *"Due to a lack of adequately powered outcomes trials demonstrating its safety and CVD benefits, renal denervation is not recommended as a first-line BP-lowering intervention for hypertension."*
- *"Renal denervation is not recommended for treating hypertension in patients with moderately to severely impaired renal function (eGFR <40 mL/min/1.73 m2) or secondary causes of hypertension, until further evidence becomes available."(McEvoy et al., 2024)*

American Heart Association (AHA) - Renal Denervation for the Treatment of Hypertension: A Scientific Statement From the American Heart Association (2024)

- *"Most but not all of the new generation of trials reached their primary end point, demonstrating modest efficacy of renal denervation in lowering blood pressure across a spectrum of hypertension, from mild to truly resistant. Individual patient responses vary, and further research is needed to identify those who may benefit most. The initial safety profile appears favorable, and multiple ongoing studies are assessing longer-*

term efficacy and safety. Multidisciplinary teams that include hypertension specialists and adequately trained proceduralists are crucial to ensure that referrals are made appropriately with full consideration of the potential risks and benefits. Incorporating patient preferences and engaging in shared decision-making conversations will help patients make the best decisions given their individual circumstances. Although further research is clearly needed, renal denervation presents a novel treatment strategy for patients with uncontrolled blood pressure." (Cluett et al., 2024)

European Society of Hypertension (ESH) - Clinical Practice Guidelines for the Management of Arterial Hypertension (2024)

- *"Renal denervation can be considered in true-resistant hypertension" (ESH, 2024)*

Society for Cardiovascular Angiography & Interventions - SCAI Position Statement on Renal Denervation for Hypertension: Patient Selection, Operator Competence, Training and Techniques, and Organizational Recommendations (2023)

- *"Device therapies targeting the renal sympathetic nervous system hold promise as adjuncts to abate or interventions to abolish HTN, depending upon the underlying severity of blood pressure elevation. Furthermore, RDN may have beneficial effects on several conditions beyond HTN that are likely to be manifestations of sympathetic imbalance including sleep apnea, left ventricular hypertrophy, albuminuria, and atrial fibrillation."*
- *"Selection criteria appropriate for renal denervation.*
    - *Patients with resistant hypertension, defined by blood pressure >130/80 mm Hg despite being on 3 medications with maximally tolerated doses from classes with outcomes data (angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers, calcium channel blockers, thiazide diuretics, and beta blockers)*
    - *Patients with uncontrolled hypertension despite attempting lifestyle modification and antihypertensive medication but who are either intolerant of additional medication or do not wish to be on additional medications and who are willing to undergo renal denervation after shared decision-making*
    - *Priority may be appropriately given to patients with higher cardiovascular risk (eg, comorbidities of coronary artery disease, diabetes, prior transient ischemic attack/cerebrovascular accident, or chronic kidney disease) who may have the greatest benefit from blood pressure reduction" (Swaminathan et al., 2023)*

British & Irish Hypertension Society, the British Cardiovascular Society, the British Cardiovascular Intervention Society, the British Society of

Interventional Radiology and the Renal Association - Joint UK Societies' 2019 Consensus Statement on Renal Denervation

- *"The JUKS concludes that there is insufficient evidence to recommend routine use of RDN for hypertension at the present time and that use of RDN should remain restricted to clinical trials." (Lobo et al., 2019)*

V. CODING INFORMATION

ICD10 Codes that may support medical necessity

I10 Essential (primary) hypertension
I15.0 Renovascular hypertension
I16.0 Hypertensive urgency
I16.1 Hypertensive emergency
I16.9 Hypertensive crisis, unspecified
I1A.0 Resistant hypertension

0338T Transcatheter renal sympathetic denervation, percutaneous approach including arterial puncture, selective catheter placement(s) renal artery(ies), fluoroscopy, contrast injection(s), intraprocedural roadmapping and radiological supervision and interpretation, including pressure gradient measurements, flush aortogram and diagnostic renal angiography when performed; unilateral *(Not covered for Medicaid)*
0339T Transcatheter renal sympathetic denervation, …bilateral *(Not Covered for Medicaid)*
C1735 Catheter(s), intravascular for renal denervation, radiofrequency, including all single use system components
C1736 Catheter(s), intravascular for renal denervation, ultrasound, including all single use system components

Not Covered
0935T Cystourethroscopy with renal pelvic sympathetic denervation, radiofrequency ablation, retrograde ureteral approach, including insertion of guide wire, selective placement of ureteral sheath(s) and multiple conformable electrodes, contrast injection(s), and fluoroscopy, bilateral

VI. REFERENCES

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