Prior Authorization Review Panel
MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: AmeriHealth Caritas Pennsylvania & Keystone First	**Submission Date**: 2/1/2025
Policy Number: ccp.1283	**Effective Date:** 2/2017 **Revision Date:** January 1, 2025
Policy Name: Renal denervation	

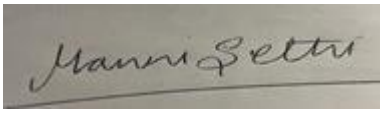
Type of Submission – Check all that apply:

- ☐ **New Policy**
- ☒ **Revised Policy***
- ☐ **Annual Review – No Revisions**
- ☐ **Statewide PDL**

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any clarifying information for the policy below:

Please see tracked changes below.

Name of Authorized Individual (Please type or print): Manni Sethi, MD, MBA, CHCQM	**Signature of Authorized Individual:** 

Keystone First
Family of Health Plans

Renal denervation

Clinical Policy ID: CCP.1283

Recent review date: 1/2025

Next review date: 5/2026

Policy contains: Renal sympathetic ablation; renal denervation; treatment-resistant hypertension.

Keystone First has developed clinical policies to assist with making coverage determinations. Keystone First's clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered by Keystone First, on a case by case basis, when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. Keystone First's clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. Keystone First's clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Keystone First will update its clinical policies as necessary. Keystone First's clinical policies are not guarantees of payment.

Coverage policy

Renal denervation for treatment-resistant hypertension is investigational/not clinically proven and, therefore, not medically necessary.

Limitations

No limitations were identified during the writing of this policy.

Alternative covered services

- Medically prescribed antihypertensive therapy.
- Standard medical treatment of underlying disorders.

Background

Hypertension is largely viewed as a major modifiable risk factor associated with mortality. The sympathetic nervous system is activated in stressful or emergency situations and often referred to as the fight-or-flight response. The kidneys play a major role in the response by increasing secretion of renin to activate a chemical chain reaction that changes the hemodynamic system of the body and provides the protective physiological response needed for a person to react. The systemic effects include arterial blood vessel constriction, increased heart rate, dilated pupils, and elevation of blood pressure (Sarathy, 2021).

Sympathetic hyperactivity-mediated resistant hypertension has been associated with multiple conditions, including but not limited to stroke, obstructive sleep apnea, metabolic syndrome, myocardial hypertrophy and heart failure, and cardiac dysrhythmias (Böhm, 2014; Hou, 2018; Sarathy, 2021). Renal injury or hypoxia can further result in systemic and renal sympathetic activity (Hou, 2018).

Renal denervation, also referred to as endovascular renal sympathetic ablation, is a minimally invasive percutaneous procedure that applies radiofrequency or focused ultrasound via a catheter inserted through the femoral artery to selectively engage the sympathetic nerve fibers surrounding the renal artery. The desired result is to interrupt the influence of the sympathetic reflexes on the kidney and systemic hemodynamics and provide a simple solution to the complex issue of hypertension (Azizi, 2023).

The procedure usually takes from 45 to 60 minutes when a single catheter is used, or less time with a multi-electrode or balloon catheter. Analgesia and sedation are required. Renal denervation has been proposed as a non-pharmacologic treatment for treatment-resistant hypertension, which is common in patients with pre-existing comorbid atherothrombotic disease and obesity, and for other sympathetically-driven conditions (Böhm, 2014).

In 2023, two renal denervation devices received pre-market approval for clinical use in the United States: Symplicity Spyral™ Renal Denervation System and Paradise® Ultrasound Renal Denervation System (U.S. Food and Drug Administration, 2023a, 2023b).").

Findings

Guidelines:

Guidelines and consensus recommendations have consistently identified renal denervation as a potential adjunctive therapy for patients with resistant or uncontrolled hypertension, albeit with caution and calls for further evidence. Position statements from the Society for Cardiovascular Angiography and Interventions reported that modest systolic blood pressure reductions of about 10 mm Hg can yield a 20% relative risk reduction in cardiovascular events, but also noted that approximately one-third of patients do not respond meaningfully to the therapy (Swaminathan, 2023).

The American Heart Association highlighted an average systolic blood pressure reduction of about 5 to 10 mm Hg, with approximately 60% to 70% of patients achieving at least a 5 mm Hg decrease by two to three months. Longer-term data from a global registry indicated sustained reductions of approximately 16 mm Hg in office measurements and 8 mm Hg by ambulatory monitoring over three years, with serious adverse events typically under 1% and no meaningful decline in renal function (Cluett, 2024; Carey, 2018). The European Society of Cardiology Council on Hypertension and the European Association of Percutaneous Cardiovascular Interventions cited durable 24-hour blood pressure reductions of clinically meaningful magnitude over up to three years without significant renal complications (Barbato, 2023).

Regulatory bodies have taken more conservative positions. The National Institute for Health and Care Excellence advised that percutaneous transluminal renal sympathetic denervation be performed only with specific governance, consent, and audit arrangements due to uncertainties in long-term benefit (NICE, 2023). Hypertension Canada did not recommend routine use, as the device was not approved in Canada, and advised that the procedure be limited to controlled clinical investigations (Hiremath, 2020).

Systematic Reviews:

A number of systematic reviews and meta-analyses have quantified the blood pressure-lowering effects of renal denervation, though effect sizes and consistency have varied. A meta-analysis of second-generation sham-controlled trials (n=1622) found statistically significant reductions in 24-hour ambulatory systolic blood pressure by -3.72 mm Hg (95% CI -5.44 to -2.00; p<0.001) and daytime systolic blood pressure by -4.10 mm Hg (95% CI -5.84 to -2.37; p<0.001). Reductions in office systolic blood pressure were also statistically significant in this analysis (-6.04 mm Hg, 95% CI -11.31 to -0.78; p=0.024), though the effect was less pronounced than for ambulatory measures; nighttime reductions did not reach statistical significance (Dantas, 2024). Another quantitative review of 15 randomized studies (n=2581) also reported statistically significant reductions in systolic and diastolic blood pressure across ambulatory, office, and home measurements (Mufarrih, 2024). A

comprehensive systematic review analyzing 25 randomized controlled trials (16 included, n = 2268) demonstrated clinically meaningful reductions in office and ambulatory systolic blood pressure across multiple subgroups (Sharp, 2024). Similarly, a meta-analysis focusing on ultrasound-based renal denervation reported mean systolic and diastolic reductions of approximately 2 to 4 mm Hg across office, daytime, nighttime, and home measurements (Maia, 2024).

Other syntheses have yielded more mixed results. A systematic review and meta-analysis of six studies (n=989) found no statistically significant difference in 24-hour ambulatory or office blood pressure compared to sham, with low certainty of evidence (Ahmed, 2023). Earlier systematic reviews and meta-analyses offered inconsistent support for renal denervation in treatment-resistant hypertension (Fadl Elmula, 2015; Shafi, 2016) and for related conditions such as Type 2 diabetes and obstructive sleep apnea (Pan, 2015; Shantha, 2015). A Cochrane review reported low- to moderate-quality evidence that did not clearly support long-term benefits (Coppolino, 2017). Additional meta-analyses published subsequently confirmed that renal denervation could safely reduce blood pressure compared to sham, but noted challenges with medication adherence and the need for improved trial design (Agasthi, 2019; Cheng, 2019; Liu, 2019; Lobo, 2019).

Randomized Controlled Trials and Device-Specific Evidence:

Randomized controlled trials have shown varied results, influenced by population characteristics, procedural techniques, and study design. The foundational SYMPLICITY trials established early evidence for renal denervation. SYMPLICITY HTN-1 (n=45) and SYMPLICITY HTN-2 (n=106) reported significant short- to medium-term office-based systolic blood pressure reductions, though these effects were smaller or inconsistent when assessed with ambulatory monitoring (Krum, 2014; Esler, 2014). The larger, sham-controlled SYMPLICITY HTN-3 trial (n=535) met safety endpoints with a major adverse event rate of only 1.4%, but failed to demonstrate statistically significant differences in blood pressure reduction compared to the sham group (Bakris, 2014; Bhatt, 2014). These studies indicated that baseline blood pressure, patient characteristics such as ethnicity and renal function, and technical proficiency might affect outcomes, prompting calls for improved trial designs and methodology (Lobo, 2015; White, 2014).

More recent trials have examined novel technologies, particularly the Paradise Ultrasound Renal Denervation System. The RADIANCE-HTN SOLO, TRIO, and RADIANCE II trials demonstrated significant reductions in daytime ambulatory systolic blood pressure at two months compared to sham, with a pooled difference of -5.9 mm Hg (95% CI -8.1 to -3.8; $p<0.001$) across the three cohorts (Azizi, 2018, 2019, 2021, 2022, 2023; Kirtane, 2023). These reductions persisted at six months, sometimes with fewer antihypertensive medications. However, the REQUIRE study (n = 143) in Japan and South Korea did not find a significant difference at three months compared to sham, potentially due to unexpected blood pressure reductions in the control group (Kario, 2022). Ongoing RCTs (SPYRAL HTN-OFF MED Pivotal and SPYRAL HTN-ON MED Expansion) are designed to address prior limitations and clarify the efficacy of renal denervation (Böhm, 2020).

Other Study Types:

Observational studies and registries have generally reported durable blood pressure reductions and favorable safety profiles. Data from global registries have shown sustained office-based systolic blood pressure reductions of approximately 16 mm Hg and ambulatory reductions of about 8 mm Hg over three years, with serious adverse events typically under 1% and no meaningful renal function deterioration (Cluett, 2024; Lee, 2019; Rodriguez-Leor, 2020; Naduvathumuriyil, 2020). Cost-effectiveness analyses, such as one by Geisler (2012), suggested potential economic value if these blood pressure reductions translate into fewer cardiovascular events. However, without definitive evidence linking renal denervation to improved long-term outcomes (e.g., stroke, myocardial infarction, heart failure), cost-effectiveness remains theoretical.

In 2025, we reorganized the findings section thematically and by evidence type. No Policy changes were warranted.

References

On December 6, 2024, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were “renal denervation,” “ablation,” “sympathectomy,” and “treatment resistant hypertension.” We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

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Policy updates

11/2016: initial review date and clinical policy effective date: 2/2017

1/2018: Policy references updated.

1/2019: Policy references updated and policy ID changed.

1/2020: Policy references updated.

1/2021: Policy references updated.

1/2022: Policy references updated.

1/2023: Policy references updated.

1/2024: Policy references updated.

1/2025: Policy references updated.