

Medicare Medical Policy

Irreversible Electroporation (IRE) (NanoKnife System)

MEDICARE MEDICAL POLICY NUMBER: 393

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INSTRUCTIONS FOR USE: Company Medicare Medical Policies serve as guidance for the administration of plan benefits and do not constitute medical advice nor a guarantee of coverage. Company Medicare Medical Policies are reviewed annually to guide the coverage or non-coverage decision-making process for services or procedures in accordance with member benefit contracts (otherwise known as Evidence of Coverage or EOCs) and Centers of Medicare and Medicaid Services (CMS) policies, manuals, and other CMS rules and regulations. In the absence of a CMS coverage determination or specific regulation for a requested service, item or procedure, Company policy criteria or applicable utilization management vendor criteria may be applied. These are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case. In cases where medical necessity is not established by policy for specific treatment modalities, evidence not previously considered regarding the efficacy of the modality that is presented shall be given consideration to determine if the policy represents current standards of care.

The Company reserves the right to determine the application of Medicare Medical Policies and make revisions to these policies at any time. Any conflict or variance between the EOC and Company Medical Policy will be resolved in favor of the EOC.

SCOPE: Providence Health Plan, Providence Health Assurance, and Providence Plan Partners as applicable (referred to individually as “Company” and collectively as “Companies”).

PRODUCT AND BENEFIT APPLICATION

Medicare Only

MEDICARE COVERAGE CRITERIA

IMPORTANT NOTE: More than one Centers for Medicare and Medicaid Services (CMS) reference may apply to the same health care service, such as when more than one coverage policy is available (e.g., both an NCD and LCD exist). All references listed should be considered for coverage decision-making. The Company uses the most current version of a Medicare reference available at the time of publication; however, these websites are not maintained by the Company, so Medicare references and their corresponding hyperlinks may change at any time. If there is a conflict between the Company Medicare Medical Policy and CMS guidance, the CMS guidance will govern.

Service	Medicare Guidelines
	<p>Medicare Coverage Criteria: “MA organizations may create publicly accessible internal coverage criteria... when coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs.” (§ 422.101(b)(6) – see Policy Guidelines below)</p> <ul style="list-style-type: none"> • Medicare Coverage Manuals: Medicare does not have criteria for irreversible electroporation (IRE) or the NanoKnife System in a coverage manual. • National Coverage Determination (NCD): Medicare does not have an NCD for IRE/NanoKnife. • Noridian J-F Local Coverage Determination (LCD)/Local Coverage Article (LCA): As of the most recent policy review, no Medicare Administrative Contractors (MACs) have LCDs for IRE/NanoKnife. • Therefore, in the absence of established Medicare coverage criteria in a manual, NCD, LCD, or other regulatory guidance for the health plan’s service area, Company criteria below are applied for medical necessity decision-making.
<p><i>Irreversible electroporation (e.g., NanoKnife System)</i></p>	<p>Company medical policy for NanoKnife System: Irreversible Electroporation (IRE)</p> <ol style="list-style-type: none"> This service is considered not medically necessary for Medicare based on the Company medical policy. <i>See Policy Guidelines below.</i>

IMPORTANT NOTICE: While some services or items may appear medically indicated for an individual, they may also be a direct exclusion of Medicare or the member’s benefit plan. Such excluded services or items by Medicare and member EOCs include, but are not limited to, services or procedures considered to be cosmetic, not medical in nature, or those considered not medically reasonable or necessary under *Title XVIII of the Social Security Act, §1862(a)(1)(A)*. If there is uncertainty regarding coverage of a service or item, please review the member EOC or submit a pre-service organization determination request. Note that the Medicare Advance Beneficiary Notice of Noncoverage (ABN) form **cannot** be used for Medicare Advantage members. (*Medicare Advance Written Notices of Non-coverage. MLN006266 May 2021*)

POLICY CROSS REFERENCES

- [Liver Tumor Treatment](#), MP265

POLICY GUIDELINES

BACKGROUND

Irreversible electroporation (IRE) is a nonthermal tissue ablation technique that permeabilizes cell membranes by delivering pulses of high-voltage, electrical current across cell membranes. This creates permanent pores in the cell membrane, which leads to cell death and tissue necrosis. The process is similar to reversible electroporation, which is used to non-lethally increase the permeability of cells to chemotherapeutic agents but uses a higher voltage. IRE may be performed percutaneously using imaging guidance or during an open or laparoscopic surgical procedure.

IRE is currently under investigational as a treatment alternative to thermal ablation techniques such as radiofrequency ablation (RFA) and microwave ablation (MWA). However, it is unclear if this alternative to thermal ablation has fewer side effects. Some known side effects specific to IRE include intense but typically transient whole-body muscular contractions and cardiac arrhythmias.

The NanoKnife System (AngioDynamics, Inc.) is a device that administers IRE, which is currently available in the United States and several countries worldwide. According to a recent Hayes review, “the NanoKnife System comprises a console with screen; generator; foot pedal; and, single-use, disposable electrode probes; and uses a proprietary algorithm to generate a treatment plan. Electrodes are placed into the tumor under computed tomography (CT) or ultrasonographic guidance. The device generates approximately 90 pulses of 1500 to 3000 volts to the tumor, with an ablation zone of ≤ 2.0 centimeters (cm). Patients are treated under general anesthesia with complete neuromuscular blockade.”¹⁻⁴

MEDICARE AND MEDICAL NECESSITY

Only medically reasonable and necessary services or items which treat illness or injury are eligible for Medicare coverage, as outlined in *Title XVIII of the Social Security Act, §1862(a)(1)(A)*. MA organizations (MAOs) make medical necessity determinations based on coverage and benefit criteria, current standards of care, the member’s unique personal medical history (e.g., diagnoses, conditions, functional status, co-morbidities, etc.), physician recommendations, and clinical notes, as well as involvement of a plan medical director, where appropriate. (*§ 422.101(c)(1)*)

“MA organizations may create publicly accessible internal coverage criteria that are based on current evidence in widely used treatment guidelines or clinical literature when coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs. Current, widely-used treatment guidelines are those developed by organizations representing clinical medical specialties, and refers to guidelines for the treatment of specific diseases or conditions. Acceptable clinical literature includes large, randomized controlled trials or prospective cohort studies with clear results, published in a peer-reviewed journal, and specifically designed to answer the relevant clinical question, or large systematic reviews or meta-analyses summarizing the literature of the specific clinical question.” (*§ 422.101(b)(6) and Medicare Managed Care Manual, Ch. 4, §90.5*)

The Company policy for *PHA Medicare Medical Policy Development and Application* (MP50) provides details regarding Medicare's definition of medical necessity and the hierarchy of Medicare references and resources during the development of medical policies, as well as the Plan's use of evidence-based processes for policy development.

There is insufficient evidence to support the use of irreversible electroporation (IRE) as a treatment for any indication, including but not limited to for treating cancer of the liver, pancreas, prostate, and kidneys. For all indications for which IRE has been proposed as a treatment, there is a limitation of randomized trials comparing IRE to other ablative treatment modalities as well as a lack of comparative data between treatment modalities, data on long-term outcomes, multicenter studies, and sufficiently large sample sizes. Furthermore, the NanoKnife System, the only IRE device identified, is currently only FDA-approved for soft tissue ablation and not for any specific tumor type. There is an ongoing FDA-approved trial regarding the use of the NanoKnife System in the treatment of prostate cancer, but it is not expected to conclude until March 2024. Therefore, the use of this IRE device for any type of cancer treatment is considered off-label. Lastly, clinical practice guidelines do not support the use of IRE for any indication.

Alternative treatments to IRE include, but may not be limited to, the following options:

- Chemotherapy
- Hormone therapy
- Prescription medication therapy
- Radiation therapy

REGULATORY STATUS

U.S. FOOD & DRUG ADMINISTRATION (FDA)

While clearance by the Food and Drug Administration (FDA) is a prerequisite for Medicare coverage, the 510(k) premarket clearance process does not in itself establish medical necessity. Medicare payment policy is determined by the interaction of numerous requirements, including but not limited to, the availability of a Medicare benefit category and other statutory requirements, coding and pricing guidelines, as well as national and local coverage determinations and clinical evidence.

The NanoKnife System (AngioDynamics Inc.) is classified as a class II device and received FDA clearance through the 510(k) clearance program in 2011 (K102329).⁵

This FDA clearance is for the surgical ablation of soft tissue. The NanoKnife System has not received clearance for the therapy or treatment of any specific disease or condition. The NanoKnife System has not received approval to market the device as a device for tumor ablation; currently, its use for treating specific types of tumors is considered off-label.¹

The NanoKnife System (AngioDynamics Inc.) is currently undergoing a clinical trial: Pivotal study of the NanoKnife System for the Ablation of Prostate Tissue in an Intermediate-Risk Population.⁶ The study began in March 2022 and expected to conclude in March 2024.

BILLING GUIDELINES AND CODING

GENERAL

There are specific CPT codes for the use of irreversible electroporation as of April, 2022. Unlisted codes are not as specific and would not be the most appropriate to bill for IRE.

CODES*		
CPT	0600T	Ablation, irreversible electroporation; 1 or more tumors per organ, including imaging guidance, when performed, percutaneous
	0601T	Ablation, irreversible electroporation; 1 or more tumors, including fluoroscopic and ultrasound guidance, when performed, open
	32999	Unlisted procedure, lungs and pleura
	47399	Unlisted procedure, liver
	48999	Unlisted procedure, pancreas
	53899	Unlisted procedure, urinary system
HCPCS	None	

*Coding Notes:

- The code list above is provided as a courtesy and may not be all-inclusive. Inclusion or omission of a code from this policy neither implies nor guarantees reimbursement or coverage. Some codes may not require routine review for medical necessity, but they are subject to provider contracts, as well as member benefits, eligibility and potential utilization audit. According to Medicare, “presence of a payment amount in the MPFS and the Medicare physician fee schedule database (MPFSDB) does not imply that CMS has determined that the service may be covered by Medicare.” The issuance of a CPT or HCPCS code or the provision of a payment or fee amount by Medicare does **not** make a procedure medically reasonable or necessary or a covered benefit by Medicare. (*Medicare Claims Processing Manual, Chapter 23 - Fee Schedule Administration and Coding Requirements, §30 - Services Paid Under the Medicare Physician’s Fee Schedule, A. Physician’s Services*)
- All unlisted codes are reviewed for medical necessity, correct coding, and pricing at the claim level. If an unlisted code is submitted for non-covered services addressed in this policy then it will be **denied as not covered**. If an unlisted code is submitted for potentially covered services addressed in this policy, to avoid post-service denial, **prior authorization is recommended**.
- **See the non-covered and prior authorization lists on the Company [Medical Policy, Reimbursement Policy, Pharmacy Policy and Provider Information website](#) for additional information.**
- HCPCS/CPT code(s) may be subject to National Correct Coding Initiative (NCCI) procedure-to-procedure (PTP) bundling edits and daily maximum edits known as “medically unlikely edits” (MUEs) published by the Centers for Medicare and Medicaid Services (CMS). This policy does not take precedence over NCCI edits or MUEs. Please refer to the CMS website for coding guidelines and applicable code combinations.

REFERENCES

1. Hayes. Health Technology Assessment. NanoKnife System for Irreversible Electroporation Treatment of Locally Advanced Pancreatic Cancer. Published: 09/01/2016. Reviewed: 08/27/2017. ARCHIVED Sep 30, 2019. Report outdated. <https://evidence.hayesinc.com/report/htb.nanoknife3033#home>. Accessed 4/18/2023.
2. He C, Huang X, Zhang Y, Cai Z, Lin X, Li S. Comparison of Survival Between Irreversible Electroporation Followed by Chemotherapy and Chemotherapy Alone for Locally Advanced Pancreatic Cancer. *Front Oncol.* 2020;10:6.
3. He C, Wang J, Sun S, et al. Irreversible electroporation versus radiotherapy after induction chemotherapy on survival in patients with locally advanced pancreatic cancer: a propensity score analysis. *BMC Cancer.* 2019;19(1):394.

4. He C, Wang J, Zhang Y, Cai Z, Lin X, Li S. Comparison of combination therapies in the management of locally advanced pancreatic cancer: Induction chemotherapy followed by irreversible electroporation vs radiofrequency ablation. *Cancer Med.* 2020;9(13):4699-4710.
5. U.S. Food & Drug Administration (FDA). NanoKnife System (AngioDynamics Inc.). Date approved: Oct 24, 2011. (K1023298) https://www.accessdata.fda.gov/cdrh_docs/pdf10/K102329.pdf. Accessed 4/18/2023.
6. U.S. National Library of Medicine. Pivotal Study of the NanoKnife System for the Ablation of Prostate Tissue (PRESERVE). Sponsored by AngioDynamics, Inc. Published July 22, 2021. Updated April 7, 2022. <https://clinicaltrials.gov/ct2/show/NCT04972097>. Accessed 4/18/2023.

POLICY REVISION HISTORY

DATE	REVISION SUMMARY
8/2023	New Medicare Advantage medical policy
6/2024	Annual review, no changes